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Bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament reconstruction (Review)

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[Intervention Review]

Bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament reconstruction

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ABSTRACT

Background

Anterior cruciate ligament (ACL) tears are frequently treated with surgical reconstruction with grafts, frequently patella tendon or hamstrings. Interference screws are often used to secure the graft in bone tunnels in the femur and tibia. This review examines whether bioabsorbable interference screws give better results than metal interference screws when used for graft fixation in ACL reconstruction.

Objectives

To assess the effects (benefits and harms) of bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction.

Search methods

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register, CENTRAL (the Cochrane Library), MEDLINE, Embase, LILACS, trial registers and reference lists of articles. Date of search: January 2016.

Selection criteria

We included randomised controlled trials and quasi-randomised trials comparing bioabsorbable with metallic interferences screws in ACL reconstruction. The main outcomes sought were subjective-rated knee function, failure of treatment, and activity level.

Data collection and analysis

At least two review authors selected eligible trials, independently assessed risk of bias, and cross-checked data. Data were pooled whenever relevant and possible. Requests for further information were sent to the original study authors.

Main results

We included 12 trials (11 randomised and one quasi-randomised) involving a total of 944 participants, and reporting follow-up results for 774. Participants in the 12 trials underwent ACL reconstruction with either hamstring tendon grafts (five trials) or patellar tendon grafts (seven trials). Trials participants were randomly allocated to bioabsorbable or metallic interference screws for graft fixation in both femur and tibia (seven trials); femur only (three trials); tibia only (one trial); location was not reported in the remaining trial. A

variety of materials was used for the bioabsorbable screws, Poly-L-lactic acid (PLLA) being the most common. The metallic screws, where reported, were titanium.

All trials were at high risk of bias, which invariably included performance bias. Seven trials were at high risk of attrition bias and eight at high risk of reporting bias. The quasi-randomised trial was assessed as being at high risk for selection bias. Based on these study limitations and insufficiency of the available data, we judged the quality of evidence for all outcomes was very low.

The majority of the available data for patient-reported knee function was presented as Lysholm scores (0 to 100; higher scores = better function). There was very low quality but consistent evidence of no clinically important differences between the two groups in Lysholm scores at 12 months follow-up (mean difference (MD) -0.08, 95% confidence interval (CI) -1.48 to 1.32; three trials, 168 participants); 24 months (MD 0.35, 95% CI -1.27 to 1.98; three trials, 113 participants) or five or more years follow-up (MD 1.23, 95% CI -2.00 to 4.47; two trials, 71 participants). This lack of between-group differences was also reported for Lysholm scores in several trials that did not provide sufficient data for pooling as well as for other self-reported knee function scores reported in several trials.

Treatment failure was represented by the summed data for implant breakage during surgery and major postoperative complications (implant failure, graft rupture, symptomatic foreign body reactions, effusion and treated arthrofibrosis and related conditions) that were usually described in the trial reports as requiring further substantive treatment. There is *very low-quality evidence* of greater treatment failure in the bioabsorbable screw group (60/451 versus 29/434; risk ratio (RR) 1.94 favouring metallic screw fixation, 95% CI 1.29 to 2.93; 885 participants, 11 studies). In a population with an assumed risk (based on the median control group risk) of 56 participants per 1000 having treatment failure after metallic screw fixation, this equates to 53 more (95% CI 17 to 108 more) per 1000 participants having treatment failure after bioabsorbable screw fixation. All 16 intraoperative complications in the bioabsorbable screw group were implant breakages upon screw insertion. Treatment failure defined as postoperative complications only still favoured the metallic screw group but the 95% CI also included the potential for a greater risk of treatment failure after metallic screw fixation: 44/451 versus 29/434; RR 1.44, 95% CI 0.93 to 2.23. Based on the assumed risk of 56 participants per 1000 having postoperative treatment failure after metallic screw fixation, this equates to 25 more (95% CI 4 fewer and 69 more) per 1000 participants having this outcome after bioabsorbable screw fixation.

There was *very low-quality evidence* of very similar activity levels in the two groups at 12 and 24 months follow-up measured via the Tegner score (0 to 10; higher scores = greater activity): 12 months (MD 0.08, 95% CI -0.39 to 0.55; 122 participants, two studies); 24 months (MD 0.01, 95% CI -0.54 to 0.57; 72 participants, two studies).

Authors' conclusions

There is *very low-quality evidence* of no difference in self-reported knee function and levels of activity between bioabsorbable and metallic interference screws for graft fixation in ACL reconstruction. There is *very low-quality evidence* that bioabsorbable screws may be associated with more overall treatment failures, including implant breakage during surgery. Further research does not appear to be a priority, but if undertaken, should also examine costs.

PLAIN LANGUAGE SUMMARY

Bioabsorbable versus metal screw for graft fixation in the surgical treatment of anterior cruciate ligament injury

Background

The anterior cruciate ligament (ACL) is a knee ligament that functions to stabilise the knee. ACL injuries are more common in athletes, such as football, basketball and handball players. Many people with ACL injuries are treated with surgery to reconstruct this ligament. In ACL reconstruction, a replacement ligament (graft) is attached to tunnels drilled into the end of the femur (thigh bone) and tibia (shin bone). Often screws are used to attach the graft to the bone. Traditionally, metal screws have been used. Although these are generally successful, metallic screws can be hard to remove if further surgery is required. They also interfere with looking at the knee using magnetic resonance imaging (MRI). With the aim of avoiding these disadvantages, and in response to patient requests, screws made from materials that dissolve over time (bioabsorbable screws) were introduced. However, such screws have been reported to have increased risks of inflammation, infection, and failed surgery.

Results of the search

We searched medical databases up to January 2016 for randomised studies comparing bioabsorbable with metal screws for graft fixation. We included 12 studies involving 944 participants undergoing surgery (ACL reconstruction).

Key results

We found evidence that self-reported measures of knee function were similar at one, two and five of more years in those treated whose grafts were fixed with bioabsorbable screws to those whose grafts were fixed with metal screws. Similarly, no differences were seen between the two types of screws in levels of activity at one and two years. However, there was evidence that bioabsorbable screws may be associated with more treatment failures. These include screw breakage during surgery, and greater numbers of graft rupture.

Quality of the evidence

All 12 studies had weaknesses that could affect the reliability of their results. We considered the evidence was *very low quality* meaning that we are unsure of these results.

Conclusions

The limited evidence does not show that knee function and activity levels are any better after bioabsorbable screws compared with metal screws. However, such screws may break during surgery and may result in a greater risk of later treatment failure. Further research does not appear to be a priority but if undertaken should also examine costs.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Bioabsorbable interference screws compared with metallic interference screws for graft fixation in ACL reconstruction

Patient or population: Adults undergoing surgical reconstruction of a ruptured ACL[1]
Settings: Hospital operating theatre
Intervention: Bioabsorbable interference screws[2] for graft fixation[3]
Comparison: Metallic interference screws (titanium, where recorded) for graft fixation[3]

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Metallic screw	Bioabsorbable screw				
Function: Lysholm knee score (0 to 100; higher scores = better function) Follow-up: 12 months	The mean Lysholm score ranged across control groups from 91 to 97.3	The mean Lysholm score in the intervention groups was 0.08 lower (1.48 lower to 1.32 higher)		168 (3 studies)	⊕◯◯◯ **very low**[4]	A similar lack of statistically significant and clinically important differences in Lysholm scores at 12 months was found in one other trial (24 participants). Trials reporting other measures of self-reported function also showed a lack of between-group differences: 2 trials (149 participants)
Function: Lysholm knee score (0 to 100; higher scores = better function) Follow-up: 24 months	The mean Lysholm score ranged across control groups from 90 to 96	The mean Lysholm score in the intervention groups was 0.35 higher (1.27 lower to 1.98 higher)		113 (3 studies)	⊕◯◯◯ **very low**[4]	A similar lack of statistically significant and clinically important differences in Lysholm scores at 24 months was found in two other

						trials (168 participants) Trials reporting other measures of self-reported function also showed a lack of between-group differences: 2 trials (77 participants)
Function: Lysholm knee score (0 to 100; higher scores = better function) Follow-up: 5 years or more	The mean Lysholm score ranged across control groups from 90 to 92	The mean Lysholm score in the intervention groups was 1.23 higher (2.00 lower to 4.47 higher)		71 (2 studies)	⊕○○○ **very low**[4]	A similar lack of statistically significant and clinically important differences in Lysholm scores at 8 years was found in one other trial (64 participants)
Overall treatment failure - Intraoperative and postoperative complications[5] Follow-up: range operative up to 7 years	**56 per 1000**[6]	**100 per 1000** (73 to 164)	**RR** 1.94 (1.29 to 2.93)	885 (11 studies)	⊕○○○ **very low**[4]	Intraoperative complications were 16 breakage of bioabsorbable screws upon insertion and one loosening of a metallic screw. Sensitivity analyses removing the dominant trial which reported 12 screw breakages or just reporting the trials with secure allocation concealment still favoured the metallic screw group
Overall treatment failure - Postoperative complications[7] Follow-up: range postoperative up to 7 years	**56 per 1000**[6]	**81 per 1000** (52 to 125)	**RR** 1.44 (0.93 to 2.23)	885 (11 studies)	⊕○○○ **very low**[4]	Note the 95% CI crosses the line of no effect and thus includes the possibility of

					a greater failure rate in the metallic screw group Graft rupture occurred twice as often in the bioabsorbable group: 12/332 versus 6/299; RR 1.70, 95% CI 0. 69 to 4.19. The difference was not statistically significant: P = 0. 25
Activity level: Tegner score (0 to 10; higher scores = greater activity) Follow-up = 12 months	The mean Tegner score ranged across control groups from 5.7 to 7.1	The mean Tegner score in the intervention groups was 0.08 higher (0.39 lower to 0.55 higher)		122 (2 studies)	⊕◯◯◯ **very low**[4]	Another trial (34 participants) found a statistically non significant difference in Tegner scores in favour of the metallic screw group at 12 months
Activity level: Tegner score (0 to 10; higher scores = greater activity) Follow-up = 24 months	The mean Tegner score ranged across control groups from 6.2 to 7.5	The mean Tegner score in the intervention groups was 0.01 higher (0.54 lower to 0.57 higher)		72 (2 studies)	⊕◯◯◯ **very low**[4]	Another trial (34 participants) found a statistically significant difference in Tegner scores of approximately 1.0 - data read off graph - in favour of the metallic screw group at 24 months

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1. Grafts used in the included trials were either hamstring or patellar tendons
2. A variety of materials was used: Poly-L-lactic acid (PLLA) was the most common
3. The randomised screws were used both in the femur and tibia in 7 trials, in the femur only in 3 trials and in the tibia only in 1 trial; unknown location in 1 trial
4. The evidence was downgraded two levels for major study limitations, reflecting high risks of performance bias and attrition bias, and one level for imprecision, reflecting small sample sizes
5. Summed data for implant breakage during surgery and major postoperative complications (implant failure, graft rupture, symptomatic foreign body reactions, effusion and treated arthrofibrosis and related conditions) that were usually described in the trial reports as requiring further substantive treatment.
6. Assumed risk is the median control risk across studies
7. Summed data for major postoperative complications (implant failure, graft rupture, symptomatic foreign body reactions, effusion and treated arthrofibrosis and related conditions) that were usually described in the trial reports as requiring further substantive treatment.

BACKGROUND

Description of the condition

The anterior cruciate ligament (ACL) is a tough band of fibrous connective tissue located within the knee joint that connects the femur (thigh bone) with the tibia (shin bone). Its primary function is to prevent the tibia from moving forward relative to the femur. It also restrains rotation of the tibia (Insall 2006).

ACL injuries, which generally occur in people participating in high-risk activities such as football, basketball, handball, or skiing, commonly involve a complete rupture of the ligament. Many people with these injuries are treated surgically by reconstructing the ligament with a graft, which can be taken from various sources. Graft choices include autografts, which are harvested from the patient, and allografts, which are grafts from cadavers. Autograft sources include the patellar tendon or quadriceps tendon (at the front of the knee) and hamstring tendons (at the back of the knee). ACL reconstruction is a common procedure that aims to restore knee function and stability and lessen the risk of subsequent knee injuries. Approximately 100,000 ACL reconstructions are performed each year in the United States (Griffin 2000).

Description of the intervention

ACL reconstruction is usually performed arthroscopically with small incisions. There are various methods of ACL reconstruction. The procedure generally involves drilling tunnels into the tibia and femur to place the ACL graft in a similar position to the native ACL. The graft is pulled up through the tibial tunnel and into the femoral tunnel. Once in position, the graft is fixed under tension using various devices. Due to its capacity to resist cyclic movements, one of the most efficient fixation devices is the interference screw. The interference screw is a conical threaded device that is inserted into the bone tunnel, compressing the graft against the tunnel walls and fixing it in the desired position. This kind of screw can be used for both femoral and tibial fixation, although it is more commonly used on the tibial side. An animation demonstrating ACL reconstruction with a patellar tendon graft is available (Zarins 2007).

Interference screws may be composed of metal or bioabsorbable materials. Once in place, metal screws are generally not removed unless there is an adverse event or removal is otherwise indicated. The advent of bioabsorbable screws resulted in part from patient preference for a device that disappears (Drogset 2005a). Bioabsorbable materials include various polymers, such as polylactic acid (PLA), poly-L-lactic acid (PLLA) or polyglycolic acid (PGA), all of which degrade and are replaced by tissue over time.

How the intervention might work

Among the most frequent surgical complications related to ACL reconstruction is arthrofibrosis, which is a restriction of knee motion in response to a fibrous scar tissue that forms when the joint remains immobile for a long time. Because the success of surgery depends on firm fixation of the reconstructed ligament in the appropriate position, devices have been developed that maintain fixation in spite of the early motion utilised in current postoperative rehabilitation techniques. Allowing this rehabilitation to start early and intensively without loss of fixation reduces the risk of arthrofibrosis and other complications. Adequate fixation, such as an interference screw, should hold the graft firmly in place for at least eight weeks (Benedetto 2000a) while the graft integrates with surrounding bone. Biomechanical studies generally have not demonstrated the superiority of one screw type over the other in regards to pullout strength (Johnson 1996; Nakano 2000; Nyland 2004; Pena 1996). In one study, Kousa 2003 concluded that bioabsorbable material performed better than metal in regard to initial pullout strength.

It is imperative that the fixation device does not cause graft breakage, damage or slippage; hardware symptoms requiring premature removal; implant breakage; infection; or other problems. Bioabsorbable fixation could reduce the need for implant removal although unabsorbed material has been found up to four years after implantation (Ma 2004). Another possible advantage is that, unlike metal screws, bioabsorbable screws do not interfere with post-surgical magnetic resonance imaging (MRI). However, some authors have reported increased incidence of synovitis (Fridén 1992) and aseptic inflammatory (foreign body) reactions from the degradation products of bioabsorbable screws (Böstman 1992; Weiler 1996). The potential for foreign body responses to bioabsorbable materials seems to depend to some extent on the polymer used (Kanon 2009). Generally, screw degradation should be accompanied by bone replacement of the defect, however, the tissue response accompanying this process is usually varied (Fink 2000).

According to Böstman 1992 , the implant might be gradually replaced by connective tissue, newly formed trabecular bone and bone marrow elements or there is a sleeve of cortical bone formed that outlines the profile of the screw while the cavity is filled with loose granulation tissue. This, though, could be advantageous in the case of ACL revision surgery and could avoid the necessity of using bone graft (Fink 2000).

Typically, metal screws cost less than bioabsorbable screws: for example, the charges in 2016 in our hospital in Brazilian real are R$ 984.00 versus R$ 1,409.00.

Why it is important to do this review

It remains unclear whether bioabsorbable screws give better results than metal screws when used to reconstruct the ACL. This review

aims to identify and appraise the best evidence available to answer this question.

OBJECTIVES

To assess and compare the effects (benefits and harms) of bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament (ACL) reconstruction.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials and quasi-randomised trials (a trial in which the allocation is not strictly random: e.g. by date of birth, hospital record number, alternation) comparing anterior cruciate ligament (ACL) reconstruction with metallic or bioabsorbable interference screws.

Types of participants

Adults undergoing surgical reconstruction of a ruptured ACL.

Types of interventions

Bioabsorbable interference screws (including polylactide (PLLA) or polyglyconate screws) versus metallic interference screws (including titanium screws) for graft fixation in any type of ACL reconstruction.

Types of outcome measures

Primary outcomes

1. Subjectively-rated knee function: wherever possible, we used validated, patient-reported function measures for the knee including those designed specifically for knee ligament injuries (the International Knee Documentation Committee - IKDC) (Irrgang 2001), the ACL Quality of Life outcome measure (Mohtadi 1998), and the Lysholm score (Lysholm 1982)); and those designed for the knee in general (Knee Injury and Osteoarthritis Outcome Score - KOOS)
2. Failure of treatment and adverse events: implant breakage, screw migration, graft loss or failure, need for revision surgery, superficial and deep infections, and symptomatic foreign body reactions. We also included arthrofibrosis, cyclops lesion and adhesions that required further surgery
3. Activity level: measured by Tegner activity level and return to sports, including time taken to resume sports

Secondary outcomes

1. Clinician-rated scores (IKDC objective score)
2. General quality of life general health measures such as the SF-36
3. Objective functional tests (e.g. single-leg hop tests)
4. Knee laxity (where possible, using the KT-arthrometer)
5. Knee range of motion
6. Pain - visual analogue scale (VAS) (Revill 1976)
7. Strength

Timing of outcome measurement

Based on the distribution of data, we decided presented results at follow-up of one year, two years and over two years (long-term results); *see* Differences between protocol and review.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (12 January 2016), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2015, Issue 12), MEDLINE (1946 to December Week 5 2015), MEDLINE In-Process & Other Non-Indexed Citations (to 11 January 2016), Embase (1980 to 2016 Week 02), and Latin American and Caribbean Health Sciences (LILACS) (1982 to 12 January 2016). We also searched the ISRCTN Registry, ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) (12 January 2016) for ongoing and recently completed trials. There were no restrictions based on language or publication status.

In MEDLINE, the sensitivity-maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials (Lefebvre 2011) was combined with the subject-specific search. The search strategies for the Cochrane Library, MEDLINE, Embase, LILACS and the trial registers are shown in Appendix 1.

Searching other resources

We checked reference lists of articles, reviews and textbooks for possible relevant studies. Whenever necessary, we also contacted researchers and experts in the field for unpublished studies.

Data collection and analysis

The intended methodology for data collection and analysis was described in our published protocol (Debieux 2012), which was based on the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2011a).

Selection of studies

Two review authors (PD and ML) independently assessed and selected potentially eligible studies for inclusion in the review. Any disagreements were resolved by discussion and, whenever necessary, by discussion with a third review author (CF). The review authors were not blinded to the journals or authors.

Data extraction and management

Two review authors (PD and ML) used a piloted data extraction form to independently collect the data. Any disagreements were resolved by a third review author (JB). Two review authors (PD and ML) entered data into Review Manager. When necessary, requests were sent to trial authors for additional information or data.

Assessment of risk of bias in included studies

Risk of bias in the included studies was independently assessed by two review authors (ML and PD). As recommended by Cochrane's 'Risk of bias' tool (Higgins 2011b). The following domains were evaluated.

1. Sequence generation (selection bias).
2. Allocation concealment (selection bias)
3. Blinding of participants and personnel (performance bias)
4. Blinding of outcome assessors (ascertainment bias)
5. Incomplete outcome data (attrition bias)
6. Selective outcome reporting bias
7. Other sources of bias (including sponsorship bias and performance bias relating to surgeon experience)

Each criterion was explicitly judged as being at either low risk of bias, high risk of bias or unclear risk of bias (either from lack of information or uncertainty over the potential for bias). Disagreements between review authors were resolved by consensus.

Measures of treatment effect

We analysed dichotomous outcome data as risk ratios (RR) with 95% confidence intervals (CIs) and continuous outcome data as mean differences with 95% CIs. When two or more studies presented their data derived from the same instrument of evaluation (with the same units of measurement), we pooled data as a mean difference (MD). Had we pooled data from studies reporting the same variables through different instruments (and different units of measurement), we would have used the standardised mean difference (SMD).

Unit of analysis issues

The unit of randomisation in the included trials was, as expected, the individual participant. As none of the trials appeared to have included people undergoing bilateral ACL reconstruction, the unit of analysis issue where data for trials were presented by knees instead of individual participants did not occur. However, we were aware of the potential for unit of analysis issues relating to outcome reporting at different times, the use of more than one screw per knee and for an estimate of overall treatment failure, where participants may have had more than one complication. For the first issue, we separately presented data at different follow-up times. For the second issue, we checked on the descriptions given for implant breakage and failure to see that these applied to screws or participants. For the third issue, we performed a sensitivity analysis to check the effect of a trial that reported a large number of intraoperative (screw breakage) complications without fully confirming whether these participants went on to have any further complications.

Overall, where such unit of analysis issues arose and appropriate corrections had not been made, we considered presenting the data for such trials only where the disparity between the units of analysis and randomisation was anticipated to be small.

Dealing with missing data

Wherever possible, we performed an intention-to-treat analysis by including all randomised patients for each intervention. We tried to contact authors of included studies in the case of missing data such as the number of events or patients, means or standard deviations. We did not carry out our plans to explore the effects of missing data via worst- and best-case scenario analyses (*see* Differences between protocol and review).

Assessment of heterogeneity

The heterogeneity of estimated effects in the included studies was assessed by visual inspection of the forest plot generated from meta-analysis of studies initially considered appropriate for pooling. The degree of statistical heterogeneity was assessed based on the test for heterogeneity and the I^2 statistic. If the results appeared to be very different or the I^2 statistic was greater than 50%, we considered this likely represented substantial heterogeneity. This information was also considered with other indicators of statistical heterogeneity, such as the chi-squared (Chi^2) statistic and degrees of freedom (df). We assumed statistically significant heterogeneity when Chi^2 exceeded df and the P value was less than 0.1.

Assessment of reporting biases

We assessed publication bias (small-study effects) by visually checking funnel plot asymmetry in meta-analyses with more than 10 studies. This was possible for a meta-analysis of overall treatment failure.

Data synthesis

If considered appropriate, results of comparable groups of trials were pooled. Initially, we used the fixed-effect model and 95% confidence intervals. However, we used the random-effects model, again with 95% confidence intervals, where substantive and unexplained heterogeneity existed.

Subgroup analysis and investigation of heterogeneity

We planned to conduct subgroup analyses to explore different surgical techniques (double-bundle versus single-bundle), different graft types (patellar tendon versus hamstrings; autograft versus allograft), different locations of interference screws (tibial versus femoral fixation of the graft), and different classes of bioabsorbable polymers. We would have investigated whether the results of subgroups were significantly different by inspecting the overlap of confidence intervals, performing the test for subgroup differences, and noting the I^2 statistic available in RevMan. However, we considered that sufficient data to accomplish these were not available.

Sensitivity analysis

Of the three pre-planned sensitivity analyses, there were sufficient data for the outcome of overall treatment failure to investigate the effects of allocation concealment, but not for the effects of including studies with a high risk of bias or of missing data. We conducted an ad hoc sensitivity analysis to check the effect of a trial that reported a large number of intraoperative (screw breakage) complications.

'Summary of findings' table

We presented the main results of the bioabsorbable versus metallic interference screws comparison in a 'Summary of findings' table. The 'Summary of findings' table provides key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on the main outcomes. We included the following primary outcomes: function using the Lysholm score (12 and 24 months) and IKDC (24 months), overall failure of treatment (intraoperative and postoperative complications; postoperative complications), and activity level using Tegner score (12 and 24 months).

We used the GRADE approach to assess the quality of evidence related to each of the above primary outcomes (section 12.2, Higgins 2011).

RESULTS

Description of studies

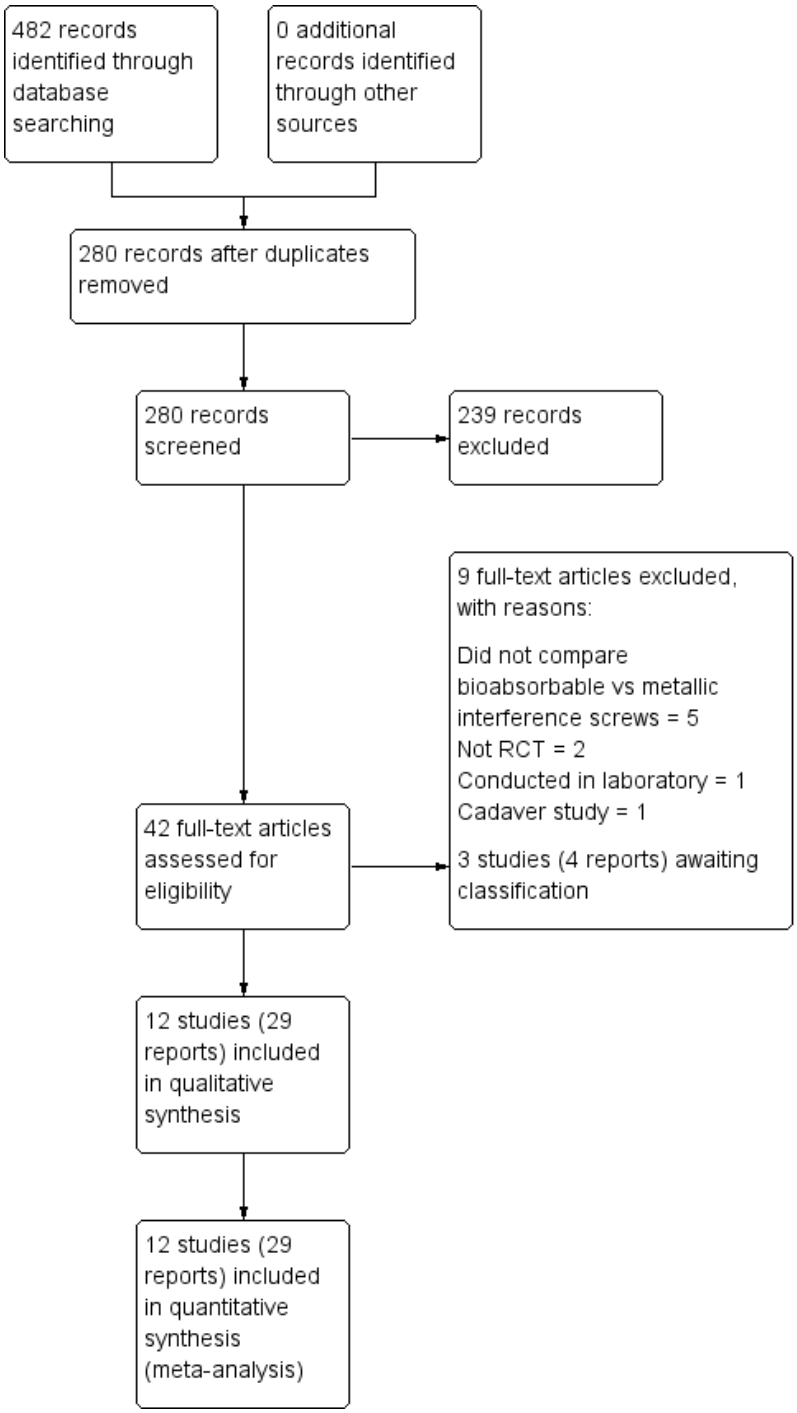
Results of the search

The search strategy (completed January 2016) identified a total of 482 records from the following databases: Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (45 records); CENTRAL (78), MEDLINE (117), Embase (140), LILACS (51), ISRCTN Registry (2), ClinicalTrials.gov (20) and the WHO International Clinical Trials Registry Platform (29). We did not obtain potentially eligible studies from any other sources.

The search resulted in the identification of the citations of 42 reports of potentially eligible studies, for which full reports were obtained where possible. We included a total of 12 studies with data published across other publications (29 reports), published between 1995 and 2015 (Arama 2015; Benedetto 2000; Drogset 2005; Fink 2000; Hegde 2014; Hofmann 2001; Järvelä 2008; Kaeding 2005; Kotani 2001; Laxdal 2006; McGuire 1995; Myers 2008). Nine studies were excluded (Barber 1999; Bourke 2013; De Wall 2011; Denti 2004; Harilainen 2009; Jagodzinski 2010; Kocabey 2003; Pł omiń ski 2008; Tecklenburg 2006) and three further studies await classification (Imbert 1999; Imhoff 1997; Toljan 1996).

A flow diagram summarising the study selection process is shown in Figure 1.

Figure 1. Study flowchart



Included studies

Details of the 12 included studies can be found in the Characteristics of included studies.

Trial reports

All 12 trials were reported in full. Seven trials were reported in two or more publications (Arama 2015: four reports; Drogset 2005: three reports; Fink 2000: two reports; Hofmann 2001: three reports; Järvelä 2008: five reports; Laxdal 2006: three reports; McGuire 1995: four reports). Single reports were available for the other five trials (Benedetto 2000; Hegde 2014; Kaeding 2005; Kotani 2001; Myers 2008). The origins of the outcome data used in this review for each of the seven trials with several publications are noted in the Characteristics of included studies. No new data were presented in the conference abstracts available for five trials (Arama 2015; Hofmann 2001; Järvelä 2008; Laxdal 2006; McGuire 1995).

Arama 2015, which included 40 participants, was reported in three conference abstracts, the first being a presentation at the AAOS annual meeting in 2007 (Pinczewski 2007). Two subsequent abstracts were published in 2012 (Pinczewski 2012a; Pinczewski 2012b), both reporting five years of follow-up. Finally, the main article was published in 2015 (Arama 2015), also with five years of follow-up.

For McGuire 1995, trial participants initially reported in the first report (McGuire 1995a) were subsequently described in three other publications. This multicentre randomised trial included several types of graft (patellar tendon, hamstrings, and allograft) and additional fixation devices that were selected for use. Of the 204 patients enrolled in the trial, 117 had reconstruction with a patellar tendon autograft (McGuire 1995a). There were two reports which started with a baseline of 114 participants who had undergone ACL reconstruction with patellar tendon (Barber 1995; Barber 2000). Barber 1995 reported on the outcome of 85 participants at a minimum of 12-month follow-up. Barber 2000 reported on 68 participants who had reached the minimum of 24-month follow-up. We chose to use data from the two reports of this subgroup (Barber 1995; Barber 2000) since the complete data are not available for the full population and this also avoids confounding where different grafts were used McGuire 1995a; McGuire 1999).

Drogset 2005 first reported on the outcome of 41 participants with two-year follow-up. With the exception of two participants in the bioabsorbable group who were excluded due to re-rupture, the outcome of the same participants was reported at seven years follow-up (Drogset 2011). Another article on the trial population reported on inflammatory mediators (C5a, TCC, and IL-8) (Drogset 2006).

Fink 2000 was reported in both English (Fink 2000) and German (Hackl 2000) publications. Both reports described the same population, methods and outcomes.

Hofmann 2001 was originally published as abstract in German (Wagner 1999). Full reports were subsequently published in German (Sudkamp 2000) and then in English (Hofmann 2001).

As explained in the Characteristics of included studies entry for Järvelä 2008, there are several publications for this trial, which compared three interventions: single-bundle reconstruction and fixation with a bioabsorbable interference screw; single-bundle reconstruction and fixation with a metallic interference screw; and double-bundle reconstruction and fixation with a bioabsorbable interference screw. In this review, we used data from 52 participants in the first two groups in the main report published in 2008 (Järvelä 2008a); and from another report of 62 participants of the first two groups published in the same year (Moisala 2008).

There are three reports for Laxdal 2006, which was published with the initial two-year follow-up in 2006. Follow-up at an average of eight years was reported at a meeting in 2009 (Stener 2009) and in an article in 2010 (Stener 2010).

Design

Eleven studies were randomised controlled trials (RCTs) and one was a quasi-randomised trial (Kaeding 2005).

Setting

Eleven studies were conducted in nine individual countries: Australia (two), Austria (one), Finland (one), Germany (one), Índia (one), Japan (one), Norway (one), Sweden (one) and USA (two). The remaining study (Benedetto 2000) was performed in two countries (Austria and the Netherlands).

Sample sizes

The included studies enrolled a total of 944 participants. The sample sizes ranged from 24 participants in Hegde 2014 to 204 participants in McGuire 1995. Outcome data were available for a total of 774 participants (82%).

Participants

Regarding gender, 574 participants were male and the gender of 14 participants was not specified. Nine studies limited the age of the participants. Two studies limited the age of the participants to over 16 years (Laxdal 2006; McGuire 1995), one study limited the age of the participants to between 15 and 50 years old (Benedetto 2000) and four studies were limited to participants with closed

physis (Fink 2000; Järvelä 2008; Kaeding 2005; Myers 2008). One study (Hegde 2014) was limited to patients between 20 and 60 years old.

Interventions

Of the 944 participants (774 assessed) for whom allocation was known, 471 were assigned to the bioabsorbable interference screw group (394 assessed) and 459 were assigned to the metallic screw group (380 assessed). The interventions, site or sites of randomisation (i.e. femur or tibia), graft used and other details of the ACL reconstruction are summarised in Table 1 and below. All operations involved single-bundle ACL reconstruction.

Regarding the type of bioabsorbable screws, six studies used poly-L-lactic acid (PLLA) (Drogset 2005; Hofmann 2001; Kaeding 2005; Kotani 2001; Laxdal 2006; McGuire 1995), two used copolymer of polyglycolic acid (PGA) and the elastomer trimethylene carbonate (PGA-TMC) (Benedetto 2000; Fink 2000), one study used copolymers composed of L-lactide, D-lactide, and trimethylene carbonate (PLLA-TMC-PDLA) (Järvelä 2008) and two used PLLA with hydroxyapatite (PLLA-HA) (Arama 2015; Myers 2008). One study did not describe the type of bioabsorbable screws used (Hegde 2014). Regarding the type of metallic screws, 10 used titanium and two (Järvelä 2008; Hegde 2014) did not mention the type of screw used.

Seven studies used the patellar tendon grafts (Benedetto 2000; Drogset 2005; Fink 2000; Hofmann 2001; Kaeding 2005; Kotani 2001; McGuire 1995) and five used hamstring tendons (Arama 2015; Hegde 2014; Järvelä 2008; Laxdal 2006; Myers 2008).

Seven studies randomised the types of screws both in the femur and tibia (Arama 2015; Järvelä 2008; Hofmann 2001; Kaeding 2005; Laxdal 2006; McGuire 1995; Myers 2008) and three (Benedetto 2000; Drogset 2005; Fink 2000) randomised screw types only in the femur. One study randomised the screw only in the tibia (Hegde 2014) and one did not mention where the randomised screw was used (Kotani 2001). Only Benedetto 2000 and McGuire 1995 used an additional tibial fixation method (staples or screws with washers) other than interference screws.

Outcome measures

The studies varied in timing of follow-up. Two studies (Benedetto 2000; Hegde 2014) specified follow-up at one year; six studies (Drogset 2005; Fink 2000; Hofmann 2001; Järvelä 2008; Kaeding 2005; McGuire 1995) specified follow-up time points between one and two years; and three studies (Kotani 2001; Laxdal 2006; Myers 2008) specified follow-up at two years. Three studies (Arama 2015; Drogset 2005; Laxdal 2006) reported extended follow-up of five years or more.

Primary outcomes

Subjectively-rated knee function

Eight studies reported the Lysholm Knee Score (Arama 2015; Drogset 2005; Fink 2000; Hegde 2014; Järvelä 2008; Laxdal 2006; Myers 2008; McGuire 1995). Drogset 2005 also reported the Knee Injury & Osteoarthritis Outcome Score (KOOS). Drogset 2005 presented data for both outcomes in graphical form only. Kotani 2001 assessed function and quality of life with two non-validated scores. The first was the ability to sit in the Japanese style and the second was the Japanese Orthopaedic Association (JOA) score.

Five studies used various versions of the International Knee Documentation Committee (IKDC) score to report on subjectively-rated knee function (Arama 2015; Benedetto 2000; Hofmann 2001; Järvelä 2008; Kaeding 2005). In Drogset 2005, participants rated their knee function according to four categories: excellent, good, fair or poor.

Treatment failure and adverse events

All studies reported on individual adverse events, to various extents, with the exception of Hegde 2014. Seven studies reported on implant failure or breakage (Arama 2015; Benedetto 2000; Hofmann 2001; Kaeding 2005; Kotani 2001; McGuire 1995; Myers 2008). Eight studies reported on infection (Arama 2015; Benedetto 2000; Drogset 2005; Fink 2000; Hofmann 2001; Kaeding 2005; Laxdal 2006; McGuire 1995). Eight studies reported graft failure or rupture (Arama 2015; Benedetto 2000; Drogset 2005; Fink 2000; Järvelä 2008; Laxdal 2006; McGuire 1995; Myers 2008). One study reported on graft damage during screw insertion (Benedetto 2000). Three studies reported on symptomatic foreign body reactions (Benedetto 2000; Kotani 2001; McGuire 1995). Six studies reported on effusion (Arama 2015; Benedetto 2000; Drogset 2005; Hofmann 2001; Kaeding 2005; McGuire 1995). Three studies reported on arthrofibrosis and surgery for cyclops lesions and adhesions (Benedetto 2000; Kotani 2001; McGuire 1995). Various other adverse events were listed in several studies, in particular for McGuire 1995, which provided a detailed summary in the text of the postoperative complications that were "reported to the Food and Drug Administration (FDA) under the requirements of the investigative device exemption (IDE) protocol".

Activity level

Five studies assessed Tegner activity level (Drogset 2005; Fink 2000; Hegde 2014; Laxdal 2006; McGuire 1995). Drogset 2005 presented data in graphical form only. Hofmann 2001 reported activity level as "the same as before", "increased," or "decreased". Kaeding 2005 assessed this outcome as "strenuous, moderate, light, and sedentary activity levels".

Secondary outcomes

Clinician-rated scores

Six studies reported results from the clinical knee examination aspect of the International Knee Documentation Committee (IKDC) score (Arama 2015; Benedetto 2000; Fink 2000; Järvelä 2008; Laxdal 2006; Myers 2008).

General quality of life general health measures

None of the studies reported these outcomes.

Objective function tests

The single-leg hop test, reported in Arama 2015 and Laxdal 2006, was the only functional test reported by any study in this review.

Knee laxity and stability

Nine studies evaluated knee laxity with the KT-1000 knee arthrometer (Arama 2015; Benedetto 2000; Drogset 2005; Fink 2000; Järvelä 2008; Kaeding 2005; Kotani 2001; Laxdal 2006; McGuire 1995), while Myers 2008 used a Rolimeter.

Knee stability was assessed via the Lachman test in six studies (Arama 2015; Benedetto 2000; Drogset 2005; Hofmann 2001; Kotani 2001; McGuire 1995) and via the pivot-shift test in seven studies (Arama 2015; Benedetto 2000; Drogset 2005; Järvelä 2008; Kotani 2001; McGuire 1995; Myers 2008).

Kotani 2001 also reported on the results of the anterior drawer stress test. Hofmann 2001 reported on the subjectively-rated stability and Kaeding 2005 on "giving way" (extreme, moderate, absent).

Knee range of motion

Hofmann 2001 and Kaeding 2005 presented continuous range of motion data for flexion and extension. Six studies (Arama 2015; Benedetto 2000; Drogset 2005; Kotani 2001; Laxdal 2006; McGuire 1995) presented numbers of participants with range of movement deficits or complications relating to loss of range of motion.

Pain

Three studies assessed pain as an outcome. Kaeding 2005 accessed pain during strenuous, moderate or sedentary activity at 12 and 24 months of follow-up. Benedetto 2000 reported persistent pain-related complications at 12 months follow-up and Hofmann 2001 reported on pain at 24 months follow-up.

Excluded studies

We excluded nine studies. Five were excluded as they did not compare bioabsorbable versus metallic interference screws (Bourke 2013; De Wall 2011; Harilainen 2009; Jagodzinski 2010; Tecklenburg 2006). Two were excluded because they were not randomised or quasi-randomised trials (Denti 2004; Pomiński 2008). We also excluded Barber 1999 because it mainly reported on a histological study involving sheep and Kocabey 2003, which was a cadaveric study. Further details are provided in Characteristics of excluded studies.

Studies awaiting classification

Three studies are awaiting classification (Imbert 1999; Imhoff 1997; Toljan 1996). An inclusion or exclusion decision could not be made for these studies because insufficient information was available. Attempts were made to contact these authors but no responses were received. Further details are provided in Characteristics of studies awaiting classification.

Ongoing study

We did not identify any ongoing studies that addressed the comparison.

Risk of bias in included studies

Summaries of our assessments are presented in Figure 2 and Figure 3.

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

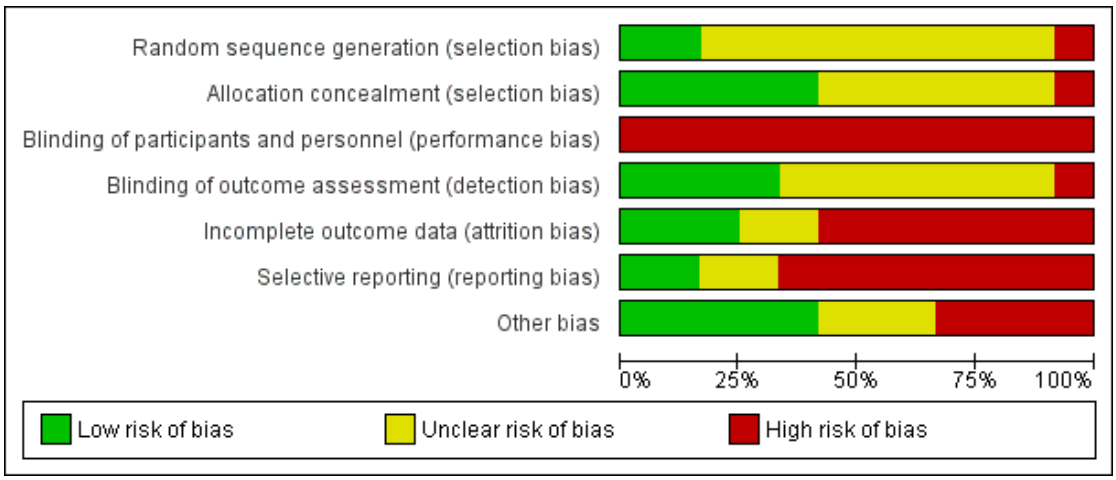
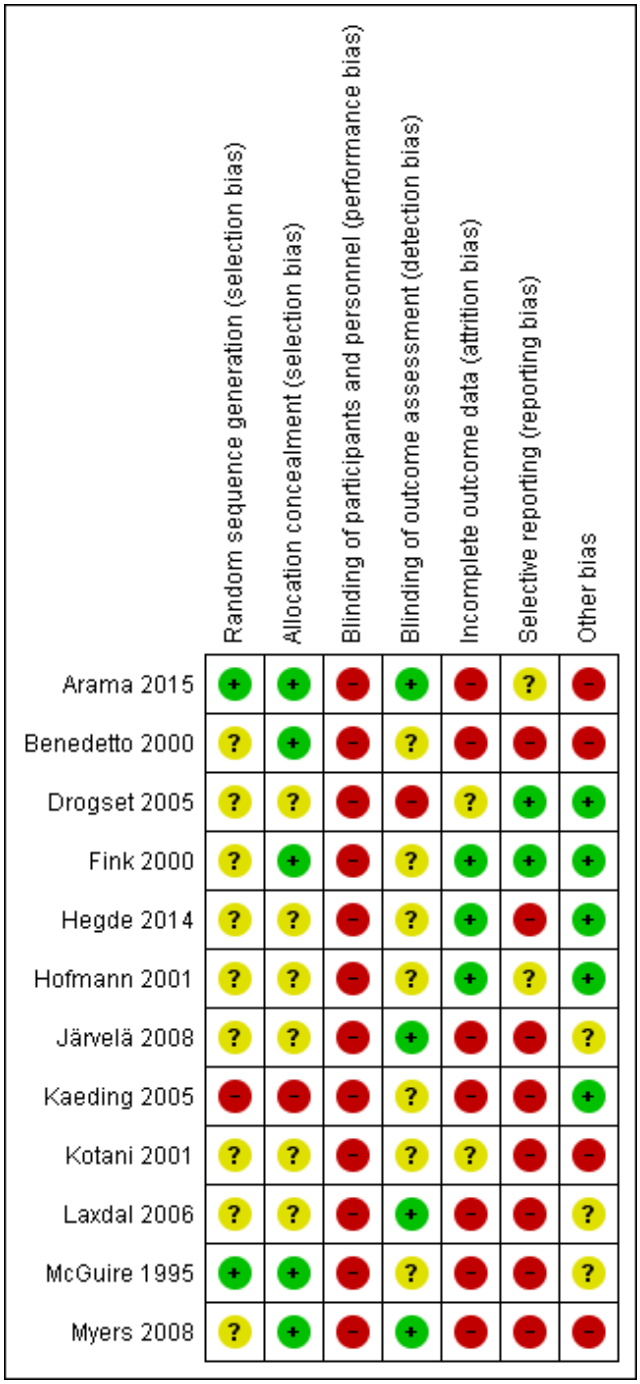


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Kaeding 2005 was quasi-randomised trial that used the last number of the patient's hospital ID; we judged this trial as having a high risk of selection bias relating to sequence generation and lack of allocation concealment. Both Arama 2015 and McGuire 1995 reported computer-based randomisation and were judged at low risk for bias relating to sequence generation. As none of the other nine included studies described their method of random sequence generation, each was assessed as at unclear risk of bias for this domain. Of the seven studies using sealed envelopes, five were assessed as having low risk of bias as they gave sufficient details that assured there was adequate allocation concealment (Arama 2015; Benedetto 2000; Fink 2000; McGuire 1995; Myers 2008*).* The other two studies (Järvelä 2008; Laxdal 2006), together with Drogset 2005, which referred to the "envelope method" without further details, were assessed at unclear risk of bias because they did not mention safeguards to ensure allocation concealment. The other three studies that reported use of randomisation without describing their methods were also rated as at unclear risk of bias *(*Hegde 2014*;* Hofmann 2001; Kotani 2001).

Blinding

Blinding of surgeons performing the operation was not possible and so all trials were assessed at high risk of performance bias. We classified the four studies that reported that blinding of outcome assessment as having a low risk of detection bias (Arama 2015; Järvelä 2008; Laxdal 2006; Myers 2008). We classified the seven studies that did not describe whether outcome assessments were blinded as having an unclear risk of detection bias (Benedetto 2000; Fink 2000; Hegde 2014; Hofmann 2001; Kaeding 2005; Kotani 2001; McGuire 1995). One study (Drogset 2005) did not blind outcome assessment and was classified as having high risk of detection bias.

Incomplete outcome data

Three studies (Benedetto 2000; Kaeding 2005; McGuire 1995) had excessive unexplained losses during follow-up. Järvelä 2008 had variable losses according to different publications; these were only partially explained. Laxdal 2006 and Myers 2008 had post-randomisation exclusions for which the reasons for exclusion were not completely explained. These six studies were assessed as having high risk of attrition bias.

It was not clear whether all randomised participants had been accounted for in Arama 2015 or Kotani 2001. This trial as well as Drogset 2005, which had a small imbalances in loss to follow-up, was assessed as having an unclear risk of attrition bias. The studies that showed no, minimal or justified losses (Fink 2000; Hegde 2014; Hofmann 2001) were assessed as having a low risk of attrition bias.

Selective reporting

Three studies presented appropriate outcomes, specifically including what our specified primary outcomes (Arama 2015; Drogset 2005; Fink 2000). Two were assessed as having a low risk of reporting bias (Drogset 2005; Fink 2000), but Arama 2015 was assessed at unclear risk given the failure to report outcome at two-year follow-up. McGuire 1995 was assessed as having a high risk of selective reporting bias given the reporting of interim results for different populations. Studies that did not present the primary outcomes, instead reporting other outcomes we considered were less relevant, were also classified as having high risk of reporting bias (Benedetto 2000; Hegde 2014; Kaeding 2005; Kotani 2001; Laxdal 2006; Myers 2008). Studies that reported primary outcomes in a partial way or using non-validated questionnaires were assessed as having an unclear risk of reporting bias (Hofmann 2001; Järvelä 2008). Additionally, we considered that the reporting in several publications of different outcomes for different sized populations at different follow-up times put Järvelä 2008 at high risk of selective reporting bias.

Other potential sources of bias

Benedetto 2000, Myers 2008 and Arama 2015 received funds from Smith & Nephew Inc., which we assessed as putting them at high risk of sponsorship bias. Kotani 2001 did not completely describe their methods and results and did not respond to our attempt to contact the authors. This study was thus assessed as having a high risk of bias. Five studies (Drogset 2005; Fink 2000; Hegde 2014; Hofmann 2001; Kaeding 2005) appeared to be free of other sources of bias. It was unclear whether the remaining studies (Järvelä 2008; Laxdal 2006; McGuire 1995) were at risk of other sources of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament reconstruction

All 12 included studies reported on the comparison that is the focus of this review: bioabsorbable versus metallic interference screw for graft fixation in ACL reconstruction. None of the planned subgroup analyses were undertaken because of insufficient data.

Bioabsorbable versus metallic interference screws

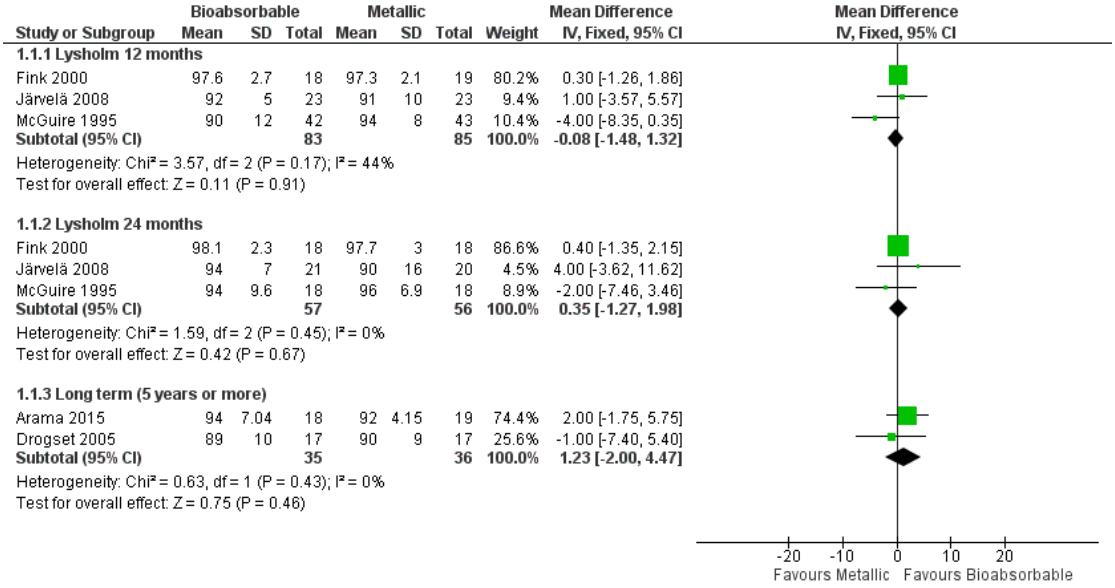
Primary outcomes

Knee function

Lysholm knee score (0 to 100; higher scores = better outcome)

None of the eight trials recording the Lysholm knee score reported a statistically significant or clinically important difference between the two groups at follow-up (Arama 2015; Drogset 2005; Fink 2000; Hegde 2014; Järvelä 2008; Laxdal 2006; Myers 2008; McGuire 1995). The available data from five trials are presented at three follow-up times in Figure 4 (Analysis 1.1). The data for McGuire 1995 are from the subgroup of participants who had patellar tendon graft reconstruction. Pooled data showed minimal differences between the two groups in the Lysholm scores at 12 months (mean difference (MD) -0.08, 95% confidence interval (CI) -1.48 to 1.32; three trials, 168 participants), at 24 months (MD 0.35, 95% CI -1.27 to 1.98; three trials, 113 participants) or at five years or more follow-up (MD 1.23, 95% CI -2.00 to 4.47; two trials, 71 participants).

Figure 4. Forest plot: 1.1 Function (Lysholm knee score: 0 to 100; higher scores = better function).



Hegde 2014 (24 participants) reported mean Lysholm scores at one-year follow-up of 84.33 in the bioabsorbable screw group and 83.67 in the metallic screw group. Laxdal 2006 reported there were no statistically significant differences between the two groups in the median Lysholm scores at either 24 months (90 versus 94; 68 participants) or at eight years follow-up (90 versus 89; 64 participants). Myers 2008 (100 participants) reported mean Lysholm scores at two years follow-up of 91.7 in the bioabsorbable screw group and 90.5 in the metallic screw group. These studies could not be pooled due to lack of available data even after attempting to contact authors.

Other self-reported function scores

Drogset 2005 (34 participants) found no difference in the Knee Injury & Osteoarthritis Outcome Score (KOOS) results at the seven-year follow-up; this was consistent with lack of between-group differences shown graphically for the five subscales of the KOOS score (pain; symptoms; activities of daily living, sports, quality of life).

Although Kaeding 2005 appears to have used the subjective evaluation of knee function using the International Knee Documentation Committee (IKDC) questionnaire, there was no report of this outcome at either one- or two-year follow-up. Järvelä 2008

presented the results of the part of subjective questionnaire that rated knee function in terms of limitations in activities of daily living (score 0 to 10; higher values = better function). They found no difference between the two groups at one- or two-year follow-up (two years: mean (SD): 9 (1) versus 9 (2); 41 participants; reported P = 0.821). Two trials reported categorical data for subjective assessment of knee function derived from the IKDC knee examination score (Benedetto 2000; Hofmann 2001) and two other trials reported on knee function based on four categories (Benedetto 2000; Drogset 2005). None of these four studies reported a difference between the two groups in acceptable knee function (rated in different ways) at the various follow-up times (e.g. 12 months: 76/80 versus 67/69; risk ratio (RR) 0.98, 95% CI 0.91 to 1.05; two trials; Analysis 1.2). Arama 2015 reported no difference between groups in subjective IKDC (0 to 100: no limitations) results at five years: bioabsorbable mean 93 (SD 11.4) versus metallic mean 93 (SD 7.0); 37 participants.

Kotani 2001 assessed function by two non-validated scores; although slightly favouring the metallic screw group, there was no significant between-groups differences at an average of 21 months in the inability to sit in the Japanese style (8/46 versus 5/45; RR 1.57, 95% CI 0.55 to 4.42) or in the Japanese Orthopaedic Association (JOA) score (0 to 100: higher scores = better outcome): MD -5.70, 95% CI -25.16 to 13.76; not shown in the analyses.

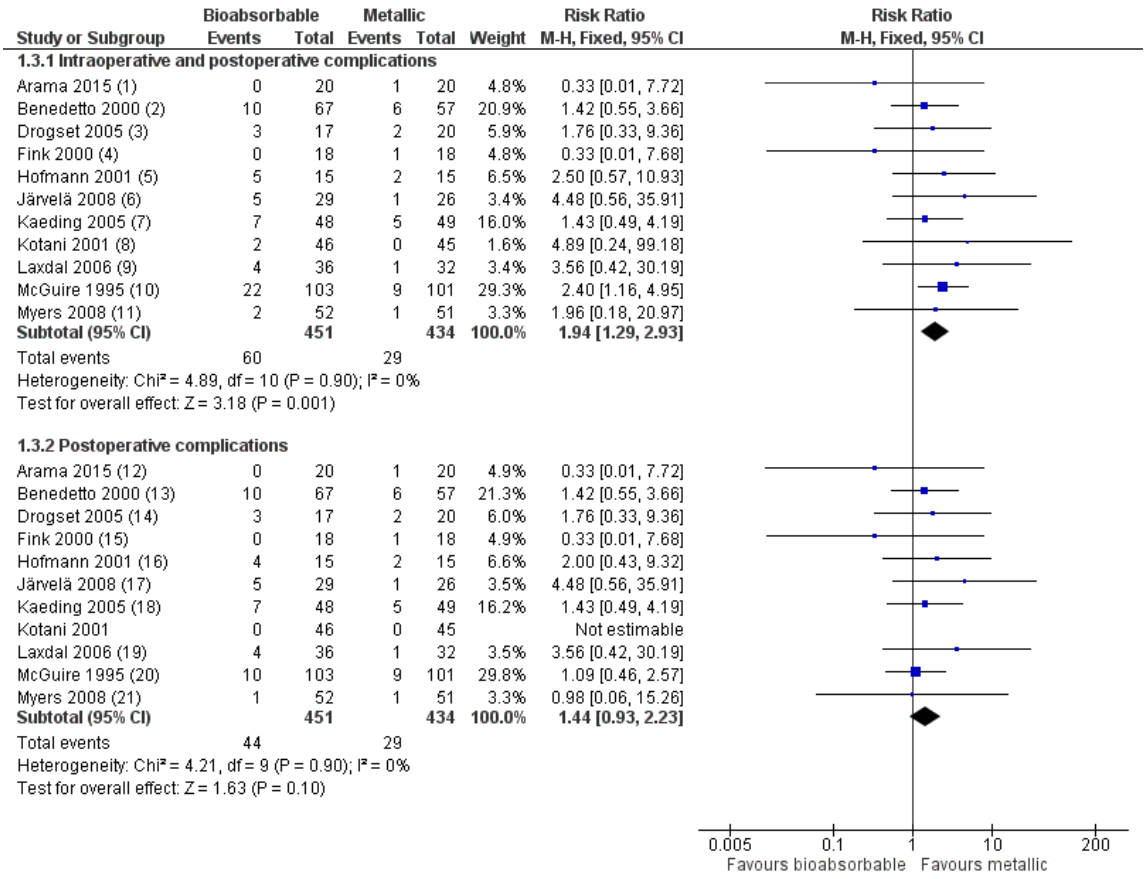
Treatment failure and adverse events

For these outcomes, we used the complete series of McGuire 1995. In interpreting the detailed list of complications provided in McGuire 1995, we extracted only those that came under our chosen categories and excluded those that appeared unrelated to the allocation of screw type. Examples of the latter are complications relating to meniscal repair and traumatic re-injuries, such as patellar fracture, that were not related to the ACL graft. Myers 2008 excluded four participants who had complications (implant breakage, graft re-rupture and persistent effusion). We have included data for the three participants for whom treatment allocation was known. Although we considered secondary procedures and surgery in our interpretation of complications, we did not present data for re-operations as these were incomplete.

Overall treatment failure and adverse events

To assess overall treatment failure, we summed data for implant breakage during surgery and major postoperative complications (implant failure, graft rupture, symptomatic foreign body reactions, effusion and treated arthrofibrosis and related conditions) that were usually described in the trial reports as requiring further substantive treatment. Pooled results for the 11 trials reporting on complications are shown in Analysis 1.3 (Figure 5). This shows there were twice as many treatment failures in the bioabsorbable screw group (60/451 versus 29/434; RR 1.94, 95% CI 1.29 to 2.93; P = 0.001). Given that these results are dominated by McGuire 1995, for which there is some uncertainty in terms of unit of analysis issues and a high intraoperative screw breakage, we performed a sensitivity analysis removing McGuire 1995. The overall result still favoured the metallic screw group (38/348 versus 20/333; RR 1.76, 95% CI 1.07 to 2.89). Another sensitivity analysis was to include only the five trials with low risk of bias related to allocation concealment; this again provided a result favouring metallic screws: 34/260 versus 18/247; 95% CI 1.73, 95% CI 1.03 to 2.93). An analysis of postoperative treatment failure also showed greater failure in the bioabsorbable screw group (44/451 versus 29/434; RR 1.44, 95% CI 0.93 to 2.23; P = 0.10); however, since the 95% CI crosses the line of no effect, these results include the possibility of a higher failure rate in the metallic group.

Figure 5. Forest plot: Overall treatment failure.

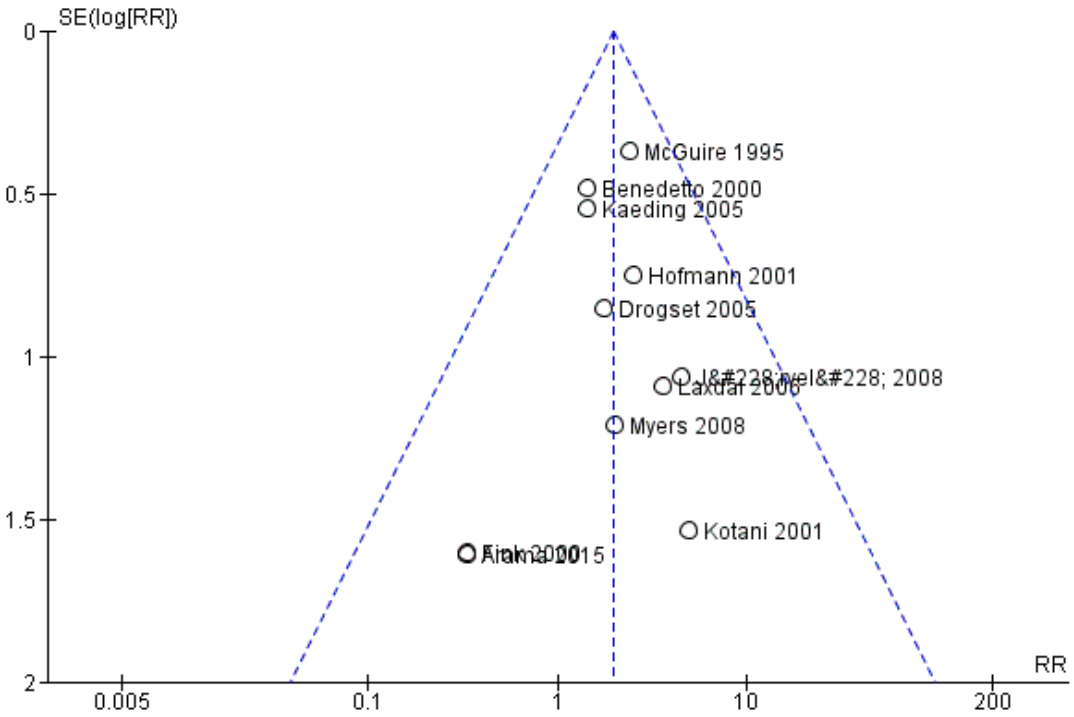


Footnotes

(1) Traumatic graft rupture; revision surgery
(2) Infection, graft tear, effusion, adhesions etc, foreign body reaction
(3) Graft rupture, effusion and infection
(4) Deep infection
(5) Infection, treated joint effusion, implant breakage
(6) Traumatic graft failure (re-injury)
(7) Infection & treated effusions
(8) Screw breakage only
(9) Graft rupture and deep infection
(10) Screw breakage, graft failure, effusion, adhesions etc
(11) Screw breakage and graft rupture
(12) Traumatic graft rupture; revision surgery
(13) Infection, graft tear, effusion, adhesions etc, foreign body reaction
(14) Graft rupture, effusion and infection
(15) Deep infection
(16) Infection, treated joint effusion
(17) Traumatic graft failure (re-injury)
(18) Infection & treated effusions
(19) Graft rupture and deep infection
(20) Graft failure, effusion, adhesions etc
(21) Graft rupture

A funnel plot analysis of intra- and postoperative treatment failure does not show asymmetry or suggest the possibility of major publication bias reflecting systematic differences between smaller and larger studies ('small-study effects') (Figure 6).

Figure 6. Funnel plot for outcome: Overall treatment failure (intra- and post-operative complications)



The results for individual complications are presented in Analysis 1.4. Only the pooled results for implant failure or breakage were statistically significant, thus meeting the P < 0.05 criterion. The incidences of graft rupture and joint effusion were higher in the bioabsorbable screw group but the results for both complications were not statistically significant and the converse finding in favour of the bioabsorbable screw are also possible.

Implant failure or breakage

This outcome applied almost exclusively to the breakage of bioabsorbable screws during surgery. Three of the six studies reporting this outcome stated that no breakage occurred (Arama 2015; Benedetto 2000; Kaeding 2005). Pooled results from seven trials show significantly greater implant failure occurred in the bioabsorbable screw group (16/351 versus 1/338; RR 6.88, 95% CI 1.85 to 25.56; P = 0.004; *see* Analysis 1.4). The evidence was dominated by McGuire 1995, which reported 12 instances of broken bioabsorbable (PLLA) screws during insertion and one metal screw that loosened and required removal. Of the 12 broken PLLA screws, the screw was left in situ in five cases, was replaced by another PLLA screw in five cases and supplemented by a metal screw in the other two cases. A report of the subgroup of participants which received a patella tendon graft, stated that all six broken screws for this subgroup were 7 mm diameter screws inserted into the femoral site (Barber 1995). Thus we have assumed that the 12 cases of broken screw applied to individual participants given that one screw was used for this location. Barber 1995 reported that the 7 mm screw was modified and a 8 mm screw made available subsequent to the conclusion of their study.

Infection

Pooled data from the eight studies reporting on infection did not reveal a difference between the two screw types (6/316 versus 6/288; RR 0.92, 95% CI 0.36 to 2.36; see Analysis 1.4).

Graft rupture

Pooled results from the eight studies reporting graft failure or rupture showed a higher incidence in the bioabsorbable screw group (12/332 versus 6/299; RR 1.70, 95% CI 0.69 to 4.19; P = 0.25; see Analysis 1.4). However, the 95% confidence interval crosses the line of no effect and thus includes the possibility of a higher graft rupture rate in the metallic group. Where details were given, all ruptures resulted from a re-injury except for a partial tear described in Benedetto 2000.

Symptomatic foreign body reactions

Three studies (Benedetto 2000; Kotani 2001; McGuire 1995) specifically referred to symptomatic foreign body reactions as an outcome. The only case, which involved a soft fluid-filled subcutaneous cyst, was reported in Benedetto 2000 (1/197 versus 0/172; RR 2.52, 95% CI 0.10 to 60.67; *see* Analysis 1.4).

Effusion

Pooled results from six studies (Arama 2015; Benedetto 2000; Drogset 2005; Hofmann 2001; Kaeding 2005; McGuire 1995) showed greater incidence of, usually treated, joint effusion in the bioabsorbable screw group (18/255 versus 11/234; RR 1.54, 95% CI 0.76 to 3.11; P = 0.23; *see* Analysis 1.4). However, the 95% confidence interval crosses the line of no effect and thus includes the possibility of a higher rate of effusion in the metallic group. The data for three trials (Benedetto 2000; Kaeding 2005; McGuire 1995) apply to 12 months follow-up, those for Drogset 2005 and Hofmann 2001 apply to 24 months follow-up and those (all 'mild') for Arama 2015 apply to five years follow-up.

Arthrofibrosis, cyclops lesions and adhesions

Pooled data from three studies reporting on arthrofibrosis and surgery for cyclops lesions and adhesions did not show a difference between the two groups (10/202 versus 11/177; RR 0.79, 95% CI 0.34 to 1.82; see Analysis 1.4).

Graft damage (during surgery)

Benedetto 2000 reported on four cases of slight damage to the graft during insertion of screws (3/67 versus 1/57) as well as slight damage to the medial femoral condyle by drilling for two participants in the bioabsorbable screw group. The clinical implications of this structural damage are unclear.

Activity level

This was reported in terms of the Tegner activity score in five trials (Drogset 2005; Fink 2000; Hegde 2014; Laxdal 2006; McGuire 1995), in terms of previous activity level in Hofmann 2001 at 12 and 24 months follow-up, and category of activity level at 12 months in Kaeding 2005.

Tegner activity score (0 to 10: higher scores = better activity)

The available data from two of the five trials reporting Tegner scores are presented at two follow-up times in Analysis 1.5. The data for McGuire 1995 are from the subgroup of participants who had patellar tendon graft reconstruction. Pooled data showed minimal differences between the two groups in the Tegner scores at 12 months (MD 0.08, 95% CI -0.39 to 0.55; 2 trials, 122 participants) and at 24 months follow-up (MD 0.01, 95% CI -0.54 to 0.57; 2 trials, 72 participants). The two-year follow-up data for 36 participants from McGuire 1995 are from a preliminary report (Barber 1995); a later report including 68 participants reported much lower but still similar scores for the two groups: 3.97 versus 3.88. Graphs presented for Drogset 2005 (34 participants) showed higher Tegner scores in the metallic screw group at 12 and 24 months and seven years follow-up; the between-group difference at two years was reported to be statistically significant (reported P < 0.05). Reading the values from the graph indicates a mean difference of just over 1.0 at this follow-up time. Hegde 2014 (24 participants) reported mean Tegner scores at one-year follow-up of 6.50 in the bioabsorbable screw group and 6.67 in the metallic screw group. Laxdal 2006 reported there was no statistically significant differences between the two groups in the median Tegner scores at either 24 months (7 versus 6; 68 participants) or at eight years follow-up (7 versus 6; 64 participants).

Other measures of activity

Hofmann 2001 (30 participants), which assessed subjectively-rated activity level as 'as before', 'increased', or 'decreased' relative to preoperative level found no difference between the two groups in those with decreased activity at one- and two-year follow-up (Analysis 1.6). Kaeding 2005 found no difference between the two groups in the distribution of activity level (strenuous, moderate, light and sedentary) at one year (97 participants) but reported a

significant difference (reported P = 0.015) in favour of the bioabsorbable screw group at two years. While fewer participants in the bioabsorbable group only participated in light or sedentary activities (5/31 versus 12/31; RR 0.46, 95% CI 0.18 to 1.15; Analysis 1.6), these data are at high risk of attrition bias given the substantial follow-up losses (33%).

Secondary outcomes

Clinician-rated scores

International Knee Documentation Committee (IKDC)

Six studies reported on the knee function results based on the primarily objective part of the International Knee Documentation Committee form (Arama 2015; Benedetto 2000; Fink 2000; Järvelä 2008; Laxdal 2006; Myers 2008). Of the five studies reporting knee function results based on the primarily objective part of the International Knee Documentation Committee form, only Myers 2008 reported on the scores. Myers 2008 found very similar IKDC objective scores (0 to 100: higher scores = better result) in the two groups at two years (mean 87.5 versus 85.2; 100 participants).

The other five studies presented their results by according to four categories (A (normal), B (nearly normal), C (abnormal), D (severely abnormal)). The available results at 12, 24 months and over five years of follow-up for the numbers of participants whose knees were rated 'normal' or 'nearly normal' are presented in Analysis 1.7. At 12 and 24 months of follow-up, there was little difference between the two groups (12 months: 80/85 versus 69/75; RR 1.03, 95% CI 0.94 to 1.12; two trials; 24 months: 62/74 versus 55/71; RR 1.09, 95% CI 0.93 to 1.27; three trials). All knees followed up at five years in Arama 2015 had normal or nearly normal results.

Objective function tests

Although Laxdal 2006 reported a significant difference (P = 0.007) at 24 months in favour of the bioabsorbable screw for the single-leg hop test, this was not reflected in the data (*see* Analysis 1.8). There was also no between-group difference at eight years follow-up (median % of non-injured side was 96 in both groups). At five years follow-up, Arama 2015 found no difference between the two groups in the number with 90% or greater performance of the single-leg hop test (*see* Analysis 1.8); all five participants with impaired performance had between 76% to 89% performance compared with the uninvolved limb.

Knee laxity and stability

Instrumental measurement of knee laxity

None of the nine studies evaluating knee laxity with the KT-1000 knee arthrometer found a difference between the two screw types at the follow-up times reported by each trial. The available continuous outcome data from eight trials are presented at four follow-up times in Analysis 1.9. The data for McGuire 1995 are from the subgroup of participants who had patellar tendon graft reconstruction. The pooled data showed minimal differences between the two groups at six months (MD -0.07 mm, 95% CI -0.53 to 0.39; 83 participants, two trials); 12 months (MD 0.06 mm, 95% CI -0.12 to 0.24; 473 participants, six trials); 24 months (MD 0.05 mm, 95% CI -0.39 to 0.49; 178 participants, four trials) or five or more years follow-up (MD -0.48 mm, 95% CI -1.39 to 0.42; 68 participants, two trials). Laxdal 2006 reported no significant between-group differences at 24 months (median 0.75 mm versus 1.5 mm; 68 participants) or at eight years follow-up (median 1.0 mm in both groups; 64 participants).

Based on a threshold of 3 mm or greater displacement measured with the KT-1000 knee arthrometer in three trials (Benedetto 2000; Drogset 2005; McGuire 1995) and the Rolimeter in Myers 2008, binary data from four trials (321 participants) at 12 months, three trials (173 participants) at 24 months and one trial (31 participants) at seven years show no difference between the two groups in the numbers of participants with knee instability (*see* Analysis 1.10).

Lachman test (positive for knee instability)

Studies evaluating knee laxity with the Lachman test (Arama 2015; Drogset 2005; Hofmann 2001; Kotani 2001; McGuire 1995) showed no significant differences between the screw types at 12 months (two trials), 24 months (29/112 versus 30/112; RR 0.97, 95% CI 0.64 to 1.49; 224 participants, four trials) or five or more years (13/33 versus 14/35; RR 0.99, 95% CI 0.56 to 1.73; 68 participants, two trials); *see* Analysis 1.10).

Pivot-shift test (positive for knee instability)

Studies evaluating knee laxity with the pivot-shift test (Arama 2015; Drogset 2005; Hofmann 2001; Kotani 2001; McGuire 1995; Myers 2008) showed no significant differences between the screw types at 12 months (29/195 versus 26/182; RR 1.08, 95% CI 0.67 to 1.73; five trials) or at 24 months (34/168 versus 29/167; RR 1.16, 95% CI 0.75 to 1.80, five trials); *see* Analysis 1.10). Although Drogset 2005 found fewer participants in the bioabsorbable group had a positive pivot-shift test at seven years (1/15 versus 5/16; RR 0.15, 95% CI 0.02 to 1.10), this result contrasted

to findings of a lack of differences for the Lachman test and instrumental laxity at seven years for the same population. Pooled data from Arama 2015 and Drogset 2005 for five or more years of follow-up also showed fewer participants in the bioabsorbable group with a positive pivot-shift test (4/33 versus 11/35; RR 0.39, 95% CI 0.13 to 1.11; two trials; P = 0.08).

Subjective reports of knee instability

Both Hofmann 2001 (30 participants) and Kaeding 2005 (65 participants at two years) found similar results in the two groups for subjective reports of instability ("giving way") (data not presented in review).

Knee range of motion

Hofmann 2001 (30 participants) reported no significant between-group differences at two years in mean flexion (95 versus 105 degrees) and mean extension (6 versus 4 degrees). Two-year follow-up results from Kaeding 2005 for 'flexion limit' and 'extension limit' also showed no clinically relevant differences between the two groups (Analysis 1.11).

Pooled data from six studies of the number of participants with range of motion deficits show little difference between the two groups (37/218 versus 28/203; RR 1.18, 95% CI 0.83 to 1.67; Analysis 1.12). Both participants in Arama 2015 with range of motion deficients had extension deficits of between 3º to 5º at five years follow-up. Two studies reported range of motion deficits as complications: Benedetto 2000 reported seven participants with poor range of motion, six of whom received subsequent surgery, and all four participants listed for Kotani 2001 had arthrofibrosis. At two years, seven participants in Drogset 2005 had extension deficits between 5 to 10 degrees; no participant had any deficit at seven years follow-up. Laxdal 2006 found no difference at two years between the two groups in the numbers with flexion deficits of at least 5 degrees, nor for extension deficits (8/33 versus 5/28). Very few participants of McGuire 1995 had either a flexion or an extension deficit. We present the data for participants with a flexion deficit (flexion < 120 degrees) at two years for the subgroup given patellar tendon grafts reported in Barber 2000.

Pain

Three studies reported separate data for long-term pain (Benedetto 2000; Hofmann 2001; Kaeding 2005). Benedetto 2000 reported on complications relating to knee pain at specific sites in the knee at 12 months. Hofmann 2001 reported participants with either mild or significant knee pain at 24 months. Pooled data showed no difference between the two groups (4/77 versus 3/67; RR 0.94, 95% CI 0.26 to 3.41; Analysis 1.13). Kaeding 2005 presented percentages of participants in the two groups who had pain during strenuous, moderate or sedentary activity at 12 and 24 months. Although the percentages added up to 100% in each case, the actual denominators were missing. Kaeding 2005 reported that pain with activity was significantly greater (P < 0.05) in the bioabsorbable group different at one-year follow-up (97 participants) but similar in the two groups at two years (65 participants); it is likely that there was one participant in each group who had pain during sedentary activities at this time.

Sensitivity analysis

Sensitivity analysis was performed for the outcome: treatment failure. More specifically, it was conducted for the outcome "intraoperative screw breakage", since McGuire 1995 disproportionately impacts the results by the number of events. Therefore, we excluded this study and re-calculated the results, noting that there was no change in the direction of the results (38/346 versus 20/332; RR 1.86, 95% CI 1.12 to 3.11).

DISCUSSION

Summary of main results

This review analysed the results of 12 trials (11 randomised and one quasi-randomised clinical trials). The studies randomised a total of 944 participants and reported follow-up results for 774 participants. Participants underwent anterior cruciate ligament (ACL) reconstruction with either hamstring tendon grafts (five trials) or patellar tendon grafts (seven trials). Trials participants were randomly allocated to bioabsorbable or metallic interference screws for graft fixation in both femur and tibia (seven trials); femur only (three trials); tibia only (one trial); location was not reported in the remaining trial.

The main results of the comparison of bioabsorbable versus metallic interference screw fixation for graft fixation in ACL reconstruction are presented in Summary of findings for the main comparison. These show a consistent picture, albeit supported by *very low-quality evidence,* of no clinically important differences between the two types of screws in self-reported knee function, measured using the Lysholm knee score, at one, two or five or more years follow-up. Treatment failure was represented by the summed data for implant breakage during surgery and major postoperative complications (implant failure, graft rupture, symptomatic foreign body reactions, knee effusion and treated arthrofibrosis and related conditions) that were usually described in the trial reports as requiring further substantive treatment. There is *very low-quality evidence* that in a population with an assumed risk (based on the median control group risk) of 56 participants per 1000 having treatment failure after metallic screw fixation, 53 more (95% CI 17 to 108 more) participants had treatment failure after bioabsorbable screw fixation. All 16 intraoperative complications in the

bioabsorbable screw group were implant breakages upon screw insertion. Treatment failure defined as postoperative complications only, still favoured the metallic screw group but the 95% CI also included the potential for a greater risk of treatment failure after metallic screw fixation. Based on the assumed risk of 56 participants per 1000 having postoperative treatment failure after metallic screw fixation, there is *very low-quality evidence* that 25 more (95% CI 4 fewer and 69 more) participants had treatment failure after bioabsorbable screw fixation. The main differences in individual complications related to graft rupture and chronic knee effusion, both of which occurred more in the bioabsorbable screw group; however, the 95% confidence interval crosses the line of no effect for both analyses and thus includes the possibility of a higher rate of these two complications in the metallic group. There was *very low-quality evidence* of very similar activity levels in the two groups at 12 and 24 months follow-up measured via the Tegner score.

Overall completeness and applicability of evidence

Although we included 12 trials that recruited 944 participants, the data available for self-reported knee function and level of activity are far fewer, declining even more at longer follow-ups. Thus, the pooled data for Lysholm scores amounted to 168 participants (18% of 944) at 12 months, 113 (12%) at 24 months and 71 (7.5%) at five or more years. 'Treatment failure' data were available for 11 trials (882 participants: 93% of total), but this outcome was only specifically reported in one trial; the data in the rest being derived from accounts of complications. Complications were poorly reported and frequently justified as a reason for excluding participants, such as those with implant breakage or reinjury (graft failure), from the analyses.

The study populations and interventions, including the grafts used for ACL reconstruction, are all relevant to current practice. Although not optimal, the outcomes collected are representative of the outcomes (Lysholm and Tegner) that are often collected in practice. Likewise, while treatment failure was inadequately reported, being specifically reported in Hofmann 2001 only, the individual complications (implant breakage, graft rupture, effusion and so on) listed are representative of those recorded in practice.

As noted by Fink 2000 and others, the bioabsorbable interference screw is more expensive that a metallic screw. This is an important consideration, but one that would be outweighed should other advantages be proven. The evidence thus far does not support the routine use of these screws, particularly in the light of greater treatment failure after bioabsorbable screw fixation. However, there will still circumstances, such as patients requiring postoperative magnetic resonance imaging (MRI) where bioabsorbable screws may be an attractive option.

Quality of the evidence

All trials were at high risk of bias, which invariably included performance bias (*see* Figure 2 and Figure 3). Seven trials were at high risk of attrition bias and eight at high risk of reporting bias. One trial, which was quasi-randomised, was at high risk for selection bias.

In our assessment of the quality of the evidence using GRADE, we downgraded the evidence for all primary outcomes, two levels because of the high risk of bias and one level for imprecision due to insufficiency of the available data. We did not downgrade for indirectness (see Overall completeness and applicability of evidence), inconsistency (there was no evidence of statistical heterogeneity) or publication bias (there were insufficient evidence to explore this but the funnel plot for treatment failure did not reveal a skewed distribution: *see* Figure 6).

Potential biases in the review process

Where possible, we performed this review in accordance with the previously published protocol; all important deviations are noted in Differences between protocol and review. While our database search was comprehensive, we did not search conference proceedings and this increases the possibility that, probably, small trials, especially those unpublished or published only in conference proceedings, may have been missed. We were careful to avoid treating different reports of the same trial as separate trials and thus avoided serious problems relating to double counting of trial participants that has occurred in other systematic reviews.

Agreements and disagreements with other studies or reviews

We identified three published meta-analyses making the same comparison (Emond 2011; Laupattarakasem 2014; Shen 2010). Emond 2011, which searched the literature between 1999 to August 2009, included eight studies, all of which appear in this review. Emond 2011 concluded that there was no difference between the metallic and bioabsorbable screws for any analysed outcome based on a strict requirement for statistical significance set at $P < 0.05$. Similar to our review, Emond 2011 noted that the treatment failures and intraoperative complications in the studies have not been well-documented. However, our review found a more pronounced result for treatment failure in favour of metallic screws.

Laupattarakasem 2014, which searched the literature between 1966 and June 2012, focused on complications and radiographic outcomes and complications, claimed to include 11 studies but actually referred to 11 articles, reporting results for eight trials. In their analyses, they inappropriately pooled results from two reports of McGuire 1995. Laupattarakasem 2014 found less implant breakage, lower effusion rates and better healing of the tunnel when metallic screw was used. The authors concluded that the

routine use of bioabsorbable fixation must be balanced according to their advantages, disadvantages and cost.

Shen 2010, which searched the literature between 1966 and December 2008, reported 10 studies, but like Laupattarakasem 2014 failed to recognise that two 'studies' were actually other reports of two studies. In their analyses, they inappropriately pooled results from two reports of Järvelä 2008. Shen 2010 concluded that joint effusion was more common in the bioabsorbable screw group, but otherwise did not find differences in other outcomes between the two types of screws.

Mascarenhas 2015 conducted a review of meta-analyses on this topic and included only the three aforementioned meta-analyses. Mascarenhas 2015 did not identify the duplicate trial publication issue for Laupattarakasem 2014 and Shen 2010. It concluded that the "best available" evidence showed "prolonged knee effusion, increased femoral tunnel widening, and increased screw breakage" with bioabsorbable interference screw use. Mascarenhas 2015 concluded that cost-effectiveness studies would be valuable but in the context of more specific situations or patient populations where the "advantages" of bioabsorbable interference screws could be used.

AUTHORS' CONCLUSIONS

Implications for practice

There is very low quality but consistent evidence of no clinically important difference in self-reported knee function at one, two and five years or more between bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament (ACL) reconstruction. A similar finding applies to levels of activity at one and two years. There is, also, very low quality but consistent evidence of greater treatment failure with bioabsorbable interference screws.

Implications for research

Given the lack of evidence to support bioabsorbable interference screws, including the potential for a greater risk of treatment failure, further randomised trials testing routine use of bioabsorbable screws compared with metallic interference screws do not appear to be a priority. If such trials are undertaken, these should conform to best design, conduct, analysis and reporting standards for randomised controlled trials and avoid major conflicts of interest. As well as careful selection of validated self-reported outcome measures, including those of knee function, such as the ACL Quality of Life outcome measure (Mohtadi 1998), and activity levels, careful monitoring and reporting of complications including overall treatment failure is required. Minimum follow-up should be two years with long-term follow-up of at least five years considered.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Arama 2015

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** The type of fixation (bioabsorbable or metal screw) was determined at the start of each procedure by opening a sealed envelope. **Assessor blinding:** Two independent assessors, unaware of the screw type, performed all preoperative and postoperative clinical assessment. **Follow-up:** 5 years. **Loss to follow-up:** 3 participants were lost to follow-up (7.5%).
Participants	**Places of study:** North Sydney Orthopaedic and Sports Medicine Centre, Sydney, Australia **Duration of the study:** Between June 2002 and October 2003. **Number of participants:** 40 participants assigned and 37 participants assessed. **Inclusion criteria:** Primary ACL reconstruction with 4-stranded hamstring graft and written informed consent to study **Exclusion criteria:** Concurrent significant other ligament injury, chondral injury, more than one-third meniscectomy, abnormal contralateral knee joint, patients seeking injury compensation **Gender:** 11 female, 29 male. **Mean age (years):** 33 years old (bioabsorbable group); 29 years old (metallic group)
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used hamstrings graft, fixed with PLLA with hydroxyapatite (PLLA-HA) screw used both in femur and tibia. **2. Metallic group:** Used hamstrings graft, fixed with titanium screw used both in femur and tibia. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** 20 bioabsorbable versus 20 metallic. **Analysed** (5 years)**:** 18 bioabsorbable versus 19 metallic.
Outcomes	**Length of follow-up:** Five years. **Primary outcomes:** • Lysholm • IKDC subjective questionnaire • Failure of treatment and adverse events: effusion, graft rupture, implant breakage, superficial and deep infections **Secondary outcomes:** • IKDC clinical examination • Functional tests: single-leg hop test • Knee stability: KT-1000; Lachman test; pivot-shift • Range of knee movement
Publications and source of data used in review	Arama 2015 was reported in three conference abstracts, one in 2007 (Pinczewski 2007) reporting 2-year follow-up and two in 2012 (Pinczewski 2012a; Pinczewski 2012b), both reporting five years follow-up. Finally, the main article was published in 2015 (Arama

	2015), also with 5 years of follow-up. Pinczewski 2007 reported 50 participants in the trial. We have accepted the number as 40 but as reported in the rest of the reports
Notes	The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted (one post randomisation exclusion) "One or more of the authors has declared the following potential conflict of interest or source of funding: Institutional research funds were received by L.A.P. from Smith & Nephew Inc."

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Patients were randomised at the time of consent via computer method." "In blocks of 20, these envelopes contained cards with the word RCI or BioRCI in equal numbers, in random order."
Allocation concealment (selection bias)	Low risk	"Each envelope was numbered consecutively on the outside. The envelopes were sealed, and there was no information on the outside of the envelope as to which card was inside. On the day before the surgery, an envelope was chosen from the box in consecutive order by the surgeon's secretary, who had no involvement in the study, and was inserted into the patients' file, which accompanied them to surgery. The envelope was opened once the patient had entered the operating room. The surgeon was then instructed as to method of fixation." Thus allocation concealment was very probably secure.
Blinding of participants and personnel (performance bias) All outcomes	High risk	While "the patients remained blinded throughout the study", the operating surgeon was not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Two independent physical therapists with extensive experience in knee assessment, unaware of the screw type, performed all preoperative and postoperative clinical assessment. The patients remained blinded throughout the study."

Arama 2015 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	An abstract published in 2007 reporting 2-year follow-up stated there were 50 participants. While small (3 out of 40) there was also some slightly inconsistent reporting of loss for follow-up at 5 years
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available. While the published reports included all expected outcomes, the clinical data for two-year follow-up were not provided
Other bias	High risk	"One or more of the authors has declared the following potential conflict of interest or source of funding: Institutional research funds were received by L.A.P. from Smith & Nephew Inc."

Benedetto 2000

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** Sealed envelopes. **Assessor blinding:** Not reported. **Follow-up:** Postoperative assessments were conducted at 3, 6, and 12 months following surgery **Loss to follow-up:** 10 participants were lost to follow-up (8%).
Participants	**Places of study:** University Hospital of Innsbruck and University Hospital of Graz, Austria; St. Joseph Ziekenhuis, Veldhoven; Carolus-Liduina Ziekenhuis, Herrogenbosch; and Medisch Centrum, Alkmaar, The Netherlands **Duration of the study:** Between August 1994 and March 1996. **Number of participants:** 124 participants assigned and 114 participants assessed. **Inclusion criteria:** Aged between 15 and 50 years requiring ACL replacement surgery in a single knee; stable knee in extension and no severe osteoarthritic changes **Exclusion criteria:** Exclusions were participants with a history of cruciate ligament injury in the unaffected knee or previous ACL surgery to either knee **Gender:** 89 female, 35 male. **Mean age (years):** 27.
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used patellar tendon graft, fixed with copolymer of polyglycolic acid (PGA) and the elastomer trimethylene carbonate (PGA-TMC) screw. In 30 cases, bioscrew was used for both femur and tibia. In 24 cases, bioscrew was used on the femur and metallic screw on the tibia. In 13 cases, additional fixation with staples was used. **2. Metallic group:** Used patellar tendon graft, fixed with titanium screw. In 41 cases the metallic screw was used both on the tibia and femur. In 16 cases, additional fixation with staples was used. The same postoperative protocol for rehabilitation was used for both groups

	Assigned: 67 bioabsorbable versus 57 metallic. **Analysed** (minimum 12 months)**:** 62 bioabsorbable versus 52 metallic.
Outcomes	**Length of follow-up:** Mean 13 months (range 10 to 22 months). **Primary outcomes:** • Subjective assessment of knee function (part of IKDC) • Failure of treatment and adverse events: effusion, re-injury, implant breakage, superficial and deep infections, symptomatic foreign body reactions to bioabsorbable screws **Secondary outcomes:** • IKDC knee examination • Knee stability: KT-1000; Lachman test; pivot-shift • Range of knee movement • Pain: assessed as either with or without pain
Publications and source of data used in review	There was just one report of this trial.
Notes	Supported by a grant from Smith & Nephew Inc. Endoscopy Division, Andovec Massachusetts The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Low risk	"Randomization to screw type was performed by opening a sealed envelope at the time of surgery."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	10 participants were withdrawn without explanation. Reasons for missing outcome data were not described. Small discrepancy: 113 participants not 114 described as followed up in text of report

Benedetto 2000 (*Continued*)

Selective reporting (reporting bias)	High risk	Authors failed to include outcomes considered as primary in this review. The study protocol is not available
Other bias	High risk	The study was supported by a grant from Smith & Nephew Inc. Endoscopy Division, Andover Massachusetts. Moreover, while the fixation on the femur was random there are several types of fixation on the tibia that were not randomised

Drogset 2005

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** Although not reported in Drogset 2005, the later trial report (Drogset 2011) describes use of envelopes. **Assessor blinding:** Not reported; states only that "The follow-ups were carried out by the first author". **Follow-up:** Participants were assessed at 6, 12, and 24 weeks and at 1 year and 2 years postoperatively (Drogset 2005). The mean follow-up time was 7.5 years in Drogset 2011. **Loss to follow-up:** 4 participants were lost to follow-up (9.7%).
Participants	**Place of study:** Department of Orthopaedics, University Hospital in Trondheim, Trondheim, Norway **Duration of the study:** June 6, 2000 to November 21, 2001. **Number of participants:** 41 participants assigned and 37 participants assessed. **Inclusion criteria:** Patients with isolated ACL ruptures or ACL ruptures with additional minor meniscal lesions and minor cartilage lesions (Outerbridge grades I and II). **Gender:** 22 female, 19 male. **Mean age (years):** 26.6.
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used patellar tendon graft, fixed with poly-L-lactic acid (PLLA) screw randomised on femur. Type of screw used in the tibia is not mentioned. **2. Metallic group:** Used patellar tendon graft, fixed with titanium screw randomised on femur. Type of screw used in the tibia is not mentioned. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** 21 bioabsorbable versus 20 metallic. **Analysed:** 18 bioabsorbable versus 19 metallic.
Outcomes	**Length of follow-up:** 2 years in Drogset 2005; mean 7.5 years in Drogset 2011. **Primary outcomes:** • Function or disability measured by: Lysholm function score • Patient-rated knee function: excellent, good, fair or poor • Activity level: Tegner • Failure of treatment and adverse events: clinical assessment of swelling, superficial and deep infections, effusion, re-rupture **Secondary outcomes:**

Drogset 2005 (*Continued*)

	• Knee stability: KT-1000; Lachman test; pivot-shift • Knee range of motion
Publications and source of data used in review	Drogset 2005 was first published with 41 randomised patients and with two-year follow-up. The same patients were followed until seven years of follow-up were available and published again (Drogset 2011). At seven-year follow-up (Drogset 2011), two patients in the bioabsorbable group were excluded due to re-rupture. In this study, the number of patients excluded (3 versus 1) was not balanced. Another study report that reported on inflammatory mediators (C5a, TCC, and IL-8) rather than clinical outcomes is also available (Drogset 2006).
Notes	The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	Drogset 2011 stated that randomisation was accomplished according to the envelope method. No mention of safeguards
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgery was carried out at our hospital by four experienced ACL surgeons. Personnel were likely not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	States that "the follow-ups were carried out by the first author."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups. One participant in the metallic group was excluded for re-rupture instead of being included in "treatment failures" (Drogset 2005). At 7-year follow-up (Drogset 2011), two participants in the bioabsorbable group were excluded for re-rupture. Also, the numbers lost to follow-up were not balanced
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes

Drogset 2005 (*Continued*)

Other bias	Low risk	The study appears to be free of other sources of bias.

Fink 2000

Methods	**Study Design:** Randomised controlled trial. **Randomisation method:** "The mode of femoral fixation (bioabsorbable or metal screw) was determined at the start of each procedure by opening a sealed envelope". **Assessor blinding:** Not reported. **Follow-up:** Participants were evaluated at 3, 6, 12, and 24 months postoperatively **Loss to follow-up:** 4 participants were lost to follow-up (10%).
Participants	**Place of study:** University Hospital for Traumatology and the Department of Radiology I, University Hospital Innsbruck, Innsbruck, Austria **Duration of the study:** Not reported. **Number of participants:** 40 participants assigned and 36 participants assessed. **Inclusion criteria:** Closed growth plates, unilateral anterior laxity confirmed clinically and with MRI, no previous knee ligament surgery, and the willingness to follow the study protocol. **Gender:** 11 female 11, 29 male. **Mean age (years):** 28.2
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used patellar tendon graft, fixed with copolymer of polyglycolic acid (PGA) and the elastomer trimethylene carbonate (PGA-TMC) screw, randomised in the femur. A metallic screw was used in the tibia in all cases. **2. Metallic group:** Used patellar tendon graft, fixed with titanium screw randomised in the femur. A metallic screw was used in the tibia in all cases. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** 20 each group. **Analysed:** 18 each group.
Outcomes	**Length of follow-up:** Follow-up was 24 months postoperatively. **Primary outcomes:** • Function or disability measured by: Lysholm function score • Failure of treatment and adverse events: assessed by deep infection • Activity Level: Tegner activity score **Secondary outcomes:** • IKDC knee examination • Knee stability: KT-1000
Publications and source of data used in review	Fink 2000 was published both in German (Hackl 2000) and English (Fink 2000). Both studies included the same group of patients who underwent the same process of randomisation and were evaluated according to the same outcomes
Notes	The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted.

Fink 2000 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Low risk	States that "the mode of femoral fixation (bioabsorbable or metal screw) was determined at the start of each procedure by opening a sealed envelope"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data were balanced in numbers across groups.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes
Other bias	Low risk	The study appears to be free of other sources of bias.

Hegde 2014

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** Not described. **Assessor blinding:** Not described whether assessors were blinded. **Follow-up:** Participants were evaluated at 3 months, 6 months and 1 year **Loss to follow-up:** No participants were lost to follow-up.
Participants	**Place of study:** Department of Orthopaedics, Yenepoya Medical College, Mangalore, India **Duration of the study:** August 2011 to July 2013. **Number of participants:** 24 participants, all assessed. **Inclusion criteria:** patients who were diagnosed to have complete ACL injuries (Grade 3); age group of 20 to 60 years **Exclusion criteria:** patients with chronic ACL insufficiency with osteoarthritis, patients with collaterals and /or PCL injuries **Gender:** all were male. **Mean age (years):** 27.8 years.

Hegde 2014 (*Continued*)

Interventions	Bioabsorbable versus metallic interference screws for distal (tibial) graft fixation in ACL reconstruction. Used quadrupled hamstring grafts, single-bundle. In all cases, endobutton was used as fixation in the femur **1. Bioabsorbable group:** Quadrupled hamstring grafts fixed with bioabsorbable screw (type not reported) in the tibia. **2. Metallic group:** quadrupled hamstring grafts, fixed with metallic screw in the tibia The postoperative protocol for rehabilitation was not reported **Assigned:** 12 each group. **Analysed:** 12 each group.
Outcomes	**Length of follow-up:** 1 year postoperatively. **Primary outcomes:** • Function: assessed by Lysholm • Activity level: assessed by Tegner activity level scale
Publications and source of data used in review	There was just one report of this trial.
Notes	The authors did not calculate the sample size.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Patients were randomly put in two groups. " The sequence generation was not described
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participants were lost to follow-up.
Selective reporting (reporting bias)	High risk	Authors failed to include outcomes considered as primary in this review. The study protocol is not available
Other bias	Low risk	The study appears to be free of other sources of bias.

Hofmann 2001

Methods	**Study Design:** Randomised controlled trial. **Randomisation method:** Not described. **Assessor blinding:** Not described. **Follow-up:** The patients were evaluated at 3, 6, 12 and 24 months postoperatively ranged from 24-32 months (average: 28 months) **Loss to follow-up:** No participants were lost to follow-up.
Participants	**Place of study:** BGU Trauma Center, Murnau, Germany. **Duration of the study:** Between April 1996 and December 1996. **Number of participants:** 30 participants assigned and 30 participants assessed. **Inclusion criteria:** Only participants with an isolated rupture of the ACL were recruited in this study **Exclusion criteria:** Meniscal tears, osteochondral lesions and other injuries, metabolic disease, alcoholism, mental disorders, previous operations on the same knee, chronic ACL injuries (more than 8 weeks). **Gender:** 6 female, 24 male. **Mean age (years):** 31.6 (range 18 to 50)
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used patellar tendon graft, fixed with poly-L-lactic acid (PLLA) screw both on the tibia and femur. **2. Metallic group:** Used patellar tendon graft, fixed with titanium screw both on the tibia and femur. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** 15 each group. **Analysed:** 15 each group.
Outcomes	**Length of follow-up:** Mean 28 months (range 24 to 32 months). **Primary outcomes:** • Failure of treatment and adverse events: infection, joint effusion, implant failure (breakage) • Activity level: as before, decreased, increased **Secondary outcomes:** • Knee function: The evaluation protocol represented a condensed form of the information contained in the knee follow-up sheets proposed by the IKDC and by Marshall et al. Categorical scale: normal, nearly normal, impaired, disturbed • Knee stability: assessed by Lachman test • Range of motion • Pain: none, mild, significant
Publications and source of data used in review	Hofmann 2001 was also originally published as abstract in 1999 in German (Wagner 1999). It was subsequently published twice: once in German (Sudkamp 2000) and then in English (Hofmann 2001).
Notes	The authors did not calculate the sample size.

Risk of bias

Bias	Authors' judgement	Support for judgement

Hofmann 2001 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	States that "30 patients were divided into both groups by a random order generated prior to the study."
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded. States that "Patients were informed about the study and the randomisation procedure."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participants were lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	No protocol. The study fails to present outcomes considered important in this review. Presents a non-validated score for quality of life evaluation and fails in proper presentation of treatment failures
Other bias	Low risk	The study appears to be free of other sources of bias.

Järvelä 2008

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** Closed envelopes. **Assessor blinding:** Clinical assessments at the final follow-up were performed by an independent and blinded examiner **Follow-up:** The patients were evaluated at 1, 3, 6, 12 and 24 months postoperatively **Loss to follow-up:** Varies, maximum 14 patients were lost to follow-up (22%).
Participants	**Places of study:** Orthopaedic Department and Arthroscopic Center, Hatanpää Hospital, Sports Clinic and Hospital Mehiläinen, Division of Orthopaedics and Traumatology, Department of Trauma, Musculoskeletal Surgery and Rehabilitation, Tampere University Hospital, Tampere University and Injury and Osteoporosis Research Center, UKK Institute, Tampere, Finland Järvelä 2008a publication **Duration of the study**: March 2003 to May 2005. **Number of participants:** 52 participants assigned and 50 assessed. Moisala 2008 publication **Duration of the study**: February 2003 to August 2005. **Number of participants:** 62 participants assigned and 55 assessed. **Inclusion criteria:** primary ACL reconstruction, closed growth plates, absence of liga-

	ment injury to the contralateral knee **Exclusion criteria:** not reported. **Gender:** 21 female, 41 male. **Mean age (years):** 32 years.
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction **1. Bioabsorbable group:** Used hamstring graft, fixed with bioabsorbable screw (L-lactide, D-lactide, and trimethylene carbonate) both on the tibia and femur. **2. Metallic group:** Used hamstring graft, fixed with titanium screw both on the tibia and femur. The same postoperative protocol for rehabilitation was used for both groups Järvelä 2008a publication **Assigned:** 27 bioabsorbable versus 25 metallic. **Analysed:** at 1-year follow-up: 23 for each group; at 2-year follow-up: 21 bioabsorbable versus 20 metallic. Moisala 2008 publication **Assigned: 31** bioabsorbable versus 31 metallic. **Analysed:** at 2-year follow-up: 29 bioabsorbable versus 26 metallic.
Outcomes	**Length of follow-up:** 24 months. **Primary outcomes:** • Knee function: assessed by Lysholm score • Subjective knee function (part of IKDC: limitations in daily activities (which might include sports), the score was 10 if there were no limitations, while the score was 0 if the patient was unable to perform his daily activities • Failure of treatment and adverse events: assessed by re-injury and re-operation **Secondary outcomes:** • IKDC knee examination • Knee stability: assessed by KT-1000, pivot-shift test
Publications and source of data used in review	There are several publications for this trial, which usually present interim data. Järvelä 2008 was published twice as an abstract (Järvelä 2005; Jarvinen 2007). The first full report was from 2005 (Järvelä 2005) and it was published again in 2007 (Jarvinen 2007) with incomplete data. One main report was published in 2008 (Järvelä 2008a); this reported on 77 participants in three groups (one group of 25 participants undergoing double-bundle reconstruction does not feature in this review). Results for the bioabsorbable versus metallic screw comparison for an extended recruitment period (62 participants) were reported in the same year (Moisala 2008). Another report of this series was published in 2012 (Suomalainen 2012), with five years of follow-up on the double-bundle versus single-bundle reconstruction comparison
Notes	The authors did not calculate the sample size. It was unclear if an intention-to-treat analysis was conducted This study includes a third group (25 participants in Järvelä 2008a) in which ACL reconstruction was performed with a double-bundle technique and fixation was accomplished with bioabsorbable interference screw. Data from this group were not included in this review Communication from Helen Handoll (24 March 2015) informed us that all these reports pertained to the same trial. This was confirmed in the Cochrane review comparing

	double versus single-bundle fixation (Tiamklung 2012).	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	States that "These patients were randomised with closed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	States that "All clinical assessments at the final follow-up were performed by an independent and blinded examiner"
Incomplete outcome data (attrition bias) All outcomes	High risk	Varies in different publications and only partly accounted for. Some post-randomisation exclusion because of complications. Imbalances between groups
Selective reporting (reporting bias)	High risk	The reporting in several publications of different outcomes for different sized populations at different follow-up times puts this trial at high risk of selective reporting bias. Also, treatment failures should have been more specifically described
Other bias	Unclear risk	The study appears to be free of other sources of bias.

Kaeding 2005

Methods	**Study design**: Quasi-randomised controlled trial. **Randomisation method:** allocation based on last digit of participant's hospital identification number. **Assessor blinding:** Not described. **Follow-up:** Participants were evaluated at 12 and 24 months postoperatively. Evaluation of activity level as well as subjective evaluation of IKDC were reported at 1 year and at 2 years **Loss to follow-up:** not reported for 1-year follow-up; 32 participants lost to 2-year follow-up (33%)
Participants	**Place of study:** Department of Orthopaedics, The Ohio State University, Columbus, Ohio; and OrthoIndy, Indianapolis, Indiana, USA **Duration of the study:** Not reported. **Number of participants:** 97 participants assessed at 1-year follow-up and 65 at 2 years. Number of patients assigned was not reported **Inclusion criteria:** Not reported. **Exclusion criteria: P**revious ACL or posterior cruciate ligament (PCL) reconstruction, multiple ligament injured knees, active infection, morbid obesity, PCL insufficiency, skeletal immaturity, history of rheumatoid arthritis or gout, prior articular or patellar fractures, multiligament-injured knees and severe degenerative joint disease. **Gender:** 32 female, 65 male. **Mean age (years):** 26.9.
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used patellar tendon graft, fixed with poly-L-lactic acid (PLLA) screw both on the tibia and femur. **2. Metallic group:** Used patellar tendon graft, fixed with titanium screw both on the tibia and femur. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** not reported. **Analysed:** 48 bioabsorbable versus 49 metallic (1 year).
Outcomes	**Length of follow-up:** The follow-up ranged from 12 and 24 months. Evaluation of activity level as well as subjective evaluation of IKDC were reported at 1 year and at 2 years. KT- 1000 arthrometer, range of motion, presence of effusions, and complications intraoperatively or postoperatively were also reported at 1 and 2 years **Primary outcomes:** • Function: assessed by subjective evaluation using the IKDC (no results reported) • Failure of treatment and adverse events: implant breakage, superficial and deep infection, effusion (none, mild), swelling with activity (strenuous, moderate, sedentary) • Activity level: Assessed by a subjective scale (strenuous, moderate, light, sedentary) **Secondary outcomes:** • Knee stability: KT-arthrometer • Knee range of motion • Pain
Publications and source of data used in review	There was just one report of this trial.

Kaeding 2005 (*Continued*)

Notes	The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	The study was quasi-randomised. States that "All patients were randomised into 1 of 2 groups according to the last digit of their hospital identification number"
Allocation concealment (selection bias)	High risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	The study did not mention the number of patients that were allocated, so it is not possible to calculate the losses during the first 12-month follow-up Authors states that there were 33% of lost to follow-up in 24 months. Despite being balanced across groups, these losses were unexplained
Selective reporting (reporting bias)	High risk	The study protocol is not available. IKDC score was pre-specified and not described in the results section Also, the study fails to provide outcomes considered important in this review, such as Lysholm score, IKDC, Tegner or SF-36. Invalidated questionnaires were used to assess pain, activity level, giving way and effusion
Other bias	Low risk	The study appears to be free of other sources of bias.

Kotani 2001

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** Not described. **Assessor blinding:** Not described whether assessors were blinded. **Follow-up:** The average postoperative follow-up period was 20 months in the bioabsorbable group and 22 months in the metallic group **Loss to follow-up:** No participants were lost to follow-up but it is not clear if all recruited participants were recorded
Participants	**Place of study:** Department of Orthopaedic Surgery, Kyorin University School of Medicine, Shinkawa, Mitaka-shi, Tokyo, Japan **Duration of Study:** not reported. **Number of participants:** 91 participants assessed (number of patients assigned not reported) **Inclusion criteria:** not reported. **Exclusion criteria:** not reported. **Gender:** 36 female, 55 male. **Mean age (years):** 23.9
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used patellar tendon graft, fixed with poly-L-lactic acid (PLLA) screw. It is not clear if the screw was used in the tibia, femur, or both. **2. Metallic group:** Used patellar tendon graft, fixed with titanium screw. It is not clear if the screw was used in the tibia, femur, or both. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** not reported. **Analysed:** 46 bioabsorbable versus 45 metallic.
Outcomes	**Length of follow-up:** mean 21 months. **Primary outcomes** • Function and quality of life: Japanese Orthopaedic Association (JOA) score. • Failure of treatment and adverse events: synovitis and implant breakage. **Secondary outcomes** • Knee stability: KT-1000; Lachman test, pivot-shift test • Range of knee movement: arthrofibrosis
Publications and source of data used in review	There was just one report of this trial.
Notes	The authors did not calculate the sample size.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	Not described.

Kotani 2001 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Participant flow unclear. It was not clear whether any participants were lost to follow-up
Selective reporting (reporting bias)	High risk	The study protocol is not available and the authors did not pre-specify the outcomes at each time point
Other bias	High risk	The study had a potential source of bias: time of evaluations and follow-up were not described; inclusion and exclusion criteria were not described

Laxdal 2006

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** Randomisation was accomplished by using sealed envelopes. **Assessor blinding:** Two independent physical therapists who were not involved in the rehabilitation performed all the preoperative and postoperative assessments (Laxdal 2006). "The long-term follow-up was performed by only 1 of the physiotherapists" (Stener 2010). **Follow-up:** Participants were evaluated on the first postoperative day, at 6 months, and at 2 years (Laxdal 2006). Bioscrew Group, mean 99 months and metallic screw Group, mean 96 months (Stener 2010). **Loss to follow-up:** Nine participants were lost to follow-up (11.6%) in the first two years of follow-up (Laxdal 2006). Thirteen were lost to follow-up at 96 months (17%) (Stener 2010).
Participants	**Place of study:** Department of Orthopaedics, Sahlgrenska University Hospital/Östra, Göteborg, Sweden **Duration of Study:** Between January 1999 and March 2000. **Number of participants:** 77 participants assigned and 68 participants assessed (Laxdal 2006) and 64 were assessed at 96 months (Stener 2010). **Inclusion criteria:** unilateral ACL rupture verified clinically by a positive Lachman test result and positive pivot-shift test result or through a previous diagnostic arthroscopy **Exclusion criteria:** associated PCL injury, collateral ligament laxity more than +1 compared with the contralateral side, previous knee ligament surgery, contralateral knee ligament injury, radiographically verified osteoarthritis. **Gender:** 18 female, 50 male. **Mean age (years):** 26.5.

Laxdal 2006 (*Continued*)

Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used hamstring grafts, fixed with poly-L-lactic acid (PLLA) screw both in the tibia and femur. **2. Metallic group:** Used hamstring grafts, fixed with metallic screw both in the tibia and femur. All the procedures were performed by the senior author. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** 38 bioabsorbable versus 39 metallic. **Analysed:** 36 bioabsorbable versus 32 metallic.
Outcomes	**Length of follow-up:** Participants were evaluated on the first postoperative day, at 6 months, and at 2 years (Laxdal 2006) and 96 months (Stener 2010). **Primary outcomes:** • Function or disability measured by: Lysholm function score • Activity Level: Tegner activity score • Failure of Treatment ad adverse events: re-injury, infection. **Secondary outcomes:** • IKDC knee examination • Objective function tests: single-leg hop test • Knee stability: KT-1000 • Knee range of motion
Publications and source of data used in review	Laxdal 2006 was published with the initial follow-up in 2006. The authors chose to follow these patients further and their results were reported again at the American Academy of Orthopaedic Surgeons 76th Annual Meeting in 2009 (Stener 2009). The study with the final follow-up was published in 2010 (Stener 2010).
Notes	The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	"Randomisation was performed using closed envelopes".
Blinding of participants and personnel (performance bias) All outcomes	High risk	Two senior surgeons performed all the reconstructions. Participants and personnel were likely not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Laxdal 2006: "Two independent physical therapists who were not involved in the rehabilitation performed all the preoperative and postoperative assessments"

Laxdal 2006 (*Continued*)

		Stener 2010: "The long-term follow-up was performed by only 1 of the physiotherapists"
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing outcome data were not balanced in numbers across intervention. Two participants of bioabsorbable screw group were excluded because of re-rupture. Seven were excluded from the metallic screw group, one for re-rupture. The other six were not mentioned. Reasons for exclusions were partially described
Selective reporting (reporting bias)	High risk	The study protocol is not available. Failures such as implant breakage and graft lost were not mentioned or included as an outcome. Also, infection and re-rupture were described but not included as an outcome. The need for re-operation should have been described more clearly.
Other bias	Unclear risk	Both reports seemed to include the same participants. However, it is unclear if the study is free of other sources of bias

McGuire 1995

Methods	**Study design**: Randomised controlled trial. **Randomisation method**: States that "permutated block of four was used. A computer program was used to generate the randomisation of patients into the two groups. The participating clinicians were given sealed envelopes containing cards indicating into which group the patient was enrolled" (McGuire 1999). **Assessor blinding**: Not reported. **Follow-up**: One and two years (McGuire 1995a). In McGuire 1999, the average follow-up interval was 28 months (range 11 to 64 months). Average follow-up for Barber 2000 was 35 months. **Loss to follow-up**: 40 participants were lost to follow-up at 1 year (20%), 87 at 2 years (43%) (McGuire 1999).
Participants	**Places of study**: Plano Orthopedic and Sports Medicine Center, Plano, Texas; Southern Sports Medicine and Orthopaedic Center, Nashville, Tennessee; Knee and Arthroscopic Surgery, Anchorage, Alaska and the Orthopedic Specialty Hospital, Salt Lake City, Utah - USA **Duration of the study**: April 1992 to May 1994. **Number of participants:** 204 participants. There were 148 participants assessed at 1-year follow-up and 39 at 2 years in McGuire 1995a; and 164 assessed at 1 year and 117 at 2 years in McGuire 1999. For the 117 participants having patellar tendon graft, 114 participants were assigned and 85 participants assessed in Barber 1995 and Barber 2000.

	Results for these 85 participants are used in the review. **Inclusion criteria:** Unilateral knee instability, positive Lachman's and positive pivot-shift tests, KT maximum manual side-to-side differences greater than 3 mm, a minimum age of 16 years with nearly closed knee growth plates, adequate bone density, compliance with the study protocol, and a commitment for at least two years follow-up knee; no previous surgeries in the index knee, chondral lesion Outerbridge grade III, no patellofemoral symptoms, absence of systemic illnesses **Exclusion criteria:** Active infection, history of blood supply limitations and/or previous infections that could retard healing, torn PCL, prior knee ligament replacement. **Gender:** 66 female, 138 male (McGuire 1995a). **Mean age (years):** 30.0
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. Used patellar tendon graft in 117 participants, patellar tendon allograft in 59, Achilles allograft in 25, allograft together with autograft in 2, and semitendinous autograft in 1. **1. Bioabsorbable group:** Fixed with poly-L-lactic acid (PLLA) screws both in the tibia and femur in 83 patients, staples in the tibial side were used in 17 and screws with washers in 3 participants. **2. Metallic group:** Fixed with metal screws in both ends in 75 patients. In the tibial side, staples were used in 23 and screws with washers in 2 participants. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** 103 bioabsorbable versus 101 metallic. **Analysed:** 89 bioabsorbable versus 75 metallic (minimum 12 months); 61 bioabsorbable versus 56 metallic (minimum 24 months) From Barber 1995 (patellar tendon autograft only). **Assigned:** 54 bioabsorbable versus 60 metallic. **Analysed:** 51 bioabsorbable versus 59 metallic (minimum 12 months); 42 bioabsorbable versus 43 metallic (mean 19 months, range 12 to 33 months). Barber 2000: 34 in both groups (mean 35 months, range 24 to 65 months).
Outcomes	**Length of follow-up:** Postoperative assessments were recorded at one and two years (McGuire 1995a). In McGuire 1999, mean 28 months (range, 11 to 64 months). In Barber 1995, minimum 1-year follow-up; mean 35 months (range 24 to 65 months) in Barber 2000. **Primary outcomes:** • Function: Lysholm • Failure of treatment and adverse events: assessed by lytic inflammatory response and effusion, infection, implant breakage, graft loss • Activity level: Tegner score **Secondary outcomes**: • Knee stability: KT; Lachman; pivot-shift • Knee range of motion
Publications and source of data used in review	Patients reported on initially in McGuire 1995a were subsequently described in several additional publications. The study was a multicentre, randomised study that included several non-randomised types of graft (patellar tendon, hamstrings, and allograft) and additional fixation devices. The authors state that 204 participants were enrolled in the trial (McGuire 1995a). Of those, 117 underwent ACL reconstruction with patellar tendon. At a minimum of 12-month follow-up (12 to 33 months, average 19 months)

	, Barber 1995 reported on 85 of these participants. Results for the 204 participants were published at a mean 30 months follow-up in McGuire 1999. At a minimum of 24-month follow-up, 68 participants with patellar tendon autograft were available for further follow-up (Barber 2000). Results for participants treated with different graft types and different fixation devices rather than patellar tendon autografts were not included in this review
Notes	The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted. Medial collateral ligament (MCL) or lateral collateral ligament (LCL) injuries requiring repair in addition to the index procedure occurred in 15 cases, and one of these cases had an extra-articular augmentation with an iliotibial band tenodesis; ACL reconstruction with no other ligament involvement occurred in 189 cases (175 with a single graft, 14 with iliotibial band tenodesis) (McGuire 1999). In 2 cases, the bioscrew broke in fragments smaller than 1.5 cm in length, being left in situ, and supplemented with a metal screw in each case. These patients remained in the Bioscrew group, tracked for complications and had none (McGuire 1999).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	McGuire 1999: "permutated block of four was used. A computer program was used to generate the randomisation of patients into the two groups."
Allocation concealment (selection bias)	Low risk	McGuire 1999: "The participating clinicians were given sealed envelopes containing cards indicating into which group the patient was enrolled" Barber 1995**:** "Once accepted into the study, a randomised sealed envelope was opened revealing the patient's assignment to either the Bioscrew group or the metal screw group." Barber 2000**:** "Randomization was accomplished by using sealed envelope opened after acceptance into the study that revealed the patient's assignment to either the Bioscrew group or the metal screw group."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described whether assessors were blinded.

McGuire 1995 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	McGuire 1999: There were 20% of patients lost at 1 year and 43% at 2 years of follow-up Barber 1995: Missing outcome data were not balanced in numbers across intervention groups. There was unexplained lost during follow-up of 34% of patients Barber 2000: The results for only 68 participants (60%) for whom 2-year follow-up data were available were reported
Selective reporting (reporting bias)	High risk	The study protocol is not available. Although it is clear that the published reports include all expected outcomes, the reporting of interim findings could point to selective reporting bias
Other bias	Unclear risk	Both reports seemed to include the same participants. However, it is unclear if the study is free of other sources of bias

Myers 2008

Methods	**Study design**: Randomised controlled trial. **Randomisation method:** States that "patients were assigned by use of block randomisation with consecutively numbered sealed envelopes" **Assessor blinding:** The clinical assessors were blinded to the type of interference screw used in each case. **Follow-up:** The follow-up was two years. Participants were assessed preoperatively and at 3, 6, 12, and 24 months postoperatively **Loss to follow-up:** 14 patients were lost to follow-up (12.2%).
Participants	**Place of study:** Brisbane Orthopaedic and Sports Medicine Centre, Brisbane Private Hospital, Brisbane, Australia, and the Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia **Duration of Study:** February 2002 to January 2005. **Number of participants:** 114 participants assigned and 100 participants assessed. (Allocation known from 3 additional excluded participants with complications.) **Inclusion criteria:** Participants awaiting ACL reconstruction. **Exclusion criteria:** Participants with skeletal immaturity, multi-ligament injury, contralateral knee ligament injury, previous knee ligament surgery, advanced degenerative and joint disease (Outerbridge grade IV). **Gender:** 42 female, 58 male. **Mean age (years):** 30.1.
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in ACL reconstruction. **1. Bioabsorbable group:** Used hamstring grafts, fixed with PLLA with hydroxyapatite (HA-PLLA) screw both on the tibia and femur.

	2. Metallic group: Used hamstring grafts, fixed with titanium screw both on the tibia and femur. Surgery performed by one experienced surgeon and envelope was opened just prior to fixation of the graft. The same postoperative protocol for rehabilitation was used for both groups **Assigned:** not clear. **Analysed** (minimum 12 months)**:** 50 bioabsorbable versus 50 metallic. For complications including exclusions: 52 bioabsorbable versus 51 metallic
Outcomes	**Length of follow-up:** 2 years. **Primary outcomes:** • Function: Lysholm function score • Failure of treatment and adverse events: Implant breakage and re-injury **Secondary outcomes:** • IKDC knee examination • Knee stability: instrumented laxity tests, Rolimeter, pivot-shift test
Publications and source of data used in review	There was just one report of this trial.
Notes	One patient in the bioabsorbable group sustained breakage of the screw head during insertion, the patient was excluded from the study. There were 2 ruptures of autograft, 1 in each group, occurring at 6 months in the HA-PLLA group (body surfing) and at 14 months in the titanium group (soccer). These 2 participants were excluded from the final analysis Study partially funded by Smith & Nephew. The authors report no conflict of interest The authors did not calculate the sample size. It was unclear if intention-to-treat analysis was conducted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The sequence generation was not described.
Allocation concealment (selection bias)	Low risk	States that "patients were assigned by use of block randomisation with consecutively numbered sealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were likely not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The clinical assessors were blinded to the type of interference screw used in each case

Myers 2008 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	The allocation of 10 participants who were lost to follow-up was not given. There were 4 post-randomisation exclusions for complications: 2 participants with re-rupture, 1 with implant breakage and 1 with effusion linked to lupus
Selective reporting (reporting bias)	High risk	Failure of treatment was not assessed as outcome.
Other bias	High risk	The study was supported by a grant from Smith & Nephew Inc.

ACL: anterior cruciate ligament
IKDC: International Knee Documentation Committee
MRI: magnetic resonance imaging
PCL: posterior cruciate ligament
PGA: polyglycolic acid
PLLA: poly-L-lactic acid
TMC: trimethylene carbonate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Barber 1999	This study reports an histological study involving 19 sheep and results from McGuire 1995 for the subgroup reported in Barber 2000. It provides no new evidence and we chose to exclude it due to the extensive description and emphasis on basic science
Bourke 2013	This study is a randomised clinical trial comparing two types of bioabsorbable interference screws. Thus, it does not address the desired comparison of this review
De Wall 2011	This is a randomised controlled trial where tibial fixation was randomised to metal interference screw and staples or a centrally placed polyethylene screw and sheath implant. It was excluded because of the additional fixation, which was different for each type of screw
Denti 2004	Not a randomised controlled trial.
Harilainen 2009	This study is a randomised clinical trial that analysed the difference between Rigidfix cross-pin and Intrafix tibial expansion sheath with a tapered expansion screw; Rigidfix femoral and BioScrew interference screw tibial fixation, BioScrew femoral and Intrafix tibial fixation; or BioScrew fixation into both tunnels. Thus, it does not cover the comparison sought

(*Continued*)

Jagodzinski 2010	In this randomised clinical trial, participants were allocated to have their graft fixed in the tibial tunnel with either an interference screw or press-fit fixation with a bone cylinder. Thus, it does not accomplish the desired comparison
Kocabey 2003	This is a cadaveric study.
Pomin ski 2008	Not a randomised controlled trial.
Tecklenburg 2006	This study compares three types of non-metallic screws.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Imbert 1999

Methods	Method of randomisation: states random, but no description regarding methodology is provided. Assessor blinding: not mentioned Loss to follow-up: 9 cases at 12 months and 18 at 24 months.
Participants	50 participants with ACL injury requiring surgical reconstruction were included. Inclusion criteria: ACL injury Exclusion criteria: Age < 17 and > 40 years, bilateral ACL injury and repeat surgery. Country: not mentioned Period of study: not mentioned Gender: not mentioned Age: not mentioned
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament reconstruction 1. Bioresorbable intervention: states bioresorbable polylactic acid interference screw. 2. Non-resorbable intervention: states metallic titanium interference screw. Postoperative management: not mentioned
Outcomes	The following outcomes were presented: • Lysholm (states no difference, provide no details) • IKDC (states no difference, provide no details) • Tegner (states no difference, provide no details) • Radiological assessment included standard x-rays and MRI
Notes	Available only in a conference abstract. We tried unsuccessfully to contact the authors to obtain further information

Imhoff 1997

Methods	Method of randomisation: states random, but no descriptions regarding methodology is provided. Assessor blinding: not mentioned Loss to follow-up: 17 in the bioresorbable group (35%) and 10 in the control group (21%) after one year
Participants	96 participants with ACL injury requiring surgical reconstruction were included. Inclusion criteria: unilateral ACL insufficiency, laxity > 3 millimetres side-to-side difference using KT-2000 Exclusion criteria: associated PCL injury, or prior knee ligament surgery. Country: Germany Period of study: April 1993 to July 1995 Gender: not mentioned Age: not mentioned
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament reconstruction 1. Bioresorbable intervention: states bioresorbable interference screw, provides no details 2. Non-resorbable intervention: states metallic interference screw, provides no details Postoperative management: not mentioned
Outcomes	The following outcomes were presented: • Complications • Functional outcome
Notes	Available only in a conference abstract. We tried unsuccessfully to contact the authors to obtain further information

Toljan 1996

Methods	Method of randomisation: states random allocation with sealed envelopes, but no description is given regarding the method used. Assessor blinding: not mentioned Lost to follow-up: None
Participants	60 participants with ACL injury were included. Inclusion criteria: not mentioned Exclusion criteria: not mentioned Country: Hungary Period of study: not mentioned Gender: not mentioned Age: not mentioned Assigned: 30 bioresorbable and 30 stainless steel.
Interventions	Bioabsorbable versus metallic interference screws for graft fixation in anterior cruciate ligament reconstruction 1. Bioabsorbable group: states bioresorbable interference screw, provides no details 2. Metallic group: states metallic interference screw, provides no details. Postoperative protocol for rehabilitation was not mentioned
Outcomes	The following outcomes were presented: • Functional outcome • Complications • MRI results

Toljan 1996 (*Continued*)

Notes	Available only in a conference abstracts. We tried unsuccessfully to contact the authors to obtain further information

ACL: anterior cruciate ligament
IKDC: International Knee Documentation Committee
MRI: magnetic resonance imaging
PCL: posterior cruciate ligament

DATA AND ANALYSES

Comparison 1. Bioabsorbable versus metallic interference screws

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Function (Lysholm knee score: 0 to 100; higher scores = better function)	5		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Lysholm 12 months	3	168	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-1.48, 1.32]
1.2 Lysholm 24 months	3	113	Mean Difference (IV, Fixed, 95% CI)	0.35 [-1.27, 1.98]
1.3 Long term (5 years or more)	2	71	Mean Difference (IV, Fixed, 95% CI)	1.23 [-2.00, 4.47]
2 Subjective assessment of knee function: normal or nearly normal/excellent or good	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 At 12 months	2	149	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.91, 1.05]
2.2 At 24 months	2	67	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.85, 1.26]
2.3 At 7 years	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.76, 1.16]
3 Overall treatment failure	11		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Intraoperative and postoperative complications	11	885	Risk Ratio (M-H, Fixed, 95% CI)	1.94 [1.29, 2.93]
3.2 Postoperative complications	11	885	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [0.93, 2.23]
4 Individual adverse events (complications)	11		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Implant failure or breakage	7	689	Risk Ratio (M-H, Fixed, 95% CI)	6.88 [1.85, 25.56]
4.2 Infection	8	604	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.36, 2.36]
4.3 Graft rupture	8	631	Risk Ratio (M-H, Fixed, 95% CI)	1.70 [0.69, 4.19]
4.4 Symptomatic foreign body reactions	3	369	Risk Ratio (M-H, Fixed, 95% CI)	2.52 [0.10, 60.67]
4.5 Joint effusion	6	489	Risk Ratio (M-H, Fixed, 95% CI)	1.54 [0.76, 3.11]
4.6 Arthrofibrosis, cyclops lesion, adhesions	3	379	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.34, 1.82]
4.7 Graft damage (during surgery)	1	124	Risk Ratio (M-H, Fixed, 95% CI)	2.55 [0.27, 23.87]
5 Activity level (Tegner scores: 0 to 10; higher scores = greater activity)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Tegner 12 months	2	122	Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.39, 0.55]
5.2 Tegner 24 months	2	72	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.54, 0.57]
6 Activity level	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.1 Decreased activity level at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Decreased activity level at 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Light or sedentary activity only at 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

7 IKDC knee examination results: normal or nearly normal	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 At 12 months	2	160	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.94, 1.12]
7.2 At 24 months	3	145	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.93, 1.27]
7.3 Long term (5 years)	1	37	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.90, 1.11]
8 Objective function tests	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1 Single-leg hop test success at 24 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Single-leg hop test success at long term (5 years)	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Knee stability: KT-1000 (mm)	8		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1 6 months	2	83	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.53, 0.39]
9.2 12 months	6	473	Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.12, 0.24]
9.3 24 months	4	178	Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.39, 0.49]
9.4 Long term (5 or more years)	2	68	Mean Difference (IV, Fixed, 95% CI)	-0.48 [-1.39, 0.42]
10 Knee instability: objective tests	8		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.1 KT-1000 or Rolimeter 3+ mm at 12 months	4	321	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.66, 1.44]
10.2 KT-1000 or Rolimeter 3+ mm at 24 months	3	173	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.56, 2.09]
10.3 KT-1000 3+ mm at 7 years	1	31	Risk Ratio (M-H, Fixed, 95% CI)	1.6 [0.56, 4.58]
10.4 Positive Lachman test at 12 months	2	118	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.53, 1.56]
10.5 Positive Lachman test at 24 months	4	224	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.64, 1.49]
10.6 Positive Lachman test long term (5 or more years)	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.56, 1.73]
10.7 Positive pivot-shift test at 12 months	5	377	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.67, 1.73]
10.8 Positive pivot-shift test at 24 months	5	335	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.75, 1.80]
10.9 Positive pivot-shift test long term (5 or more years)	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.13, 1.11]
11 Range of knee movement (degrees) at two years	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 'Flexion limit'	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 'Extension limit'	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Range of knee movement deficits	6	421	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.83, 1.67]
13 Pain (persistent)	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.26, 3.41]
14 Overall treatment failure (intraoperative and postoperative): for funnel plot	11	882	Risk Ratio (M-H, Fixed, 95% CI)	1.95 [1.29, 2.93]

ADDITIONAL TABLES

Table 1. Details of ACL reconstruction and interventions used in the included studies

Study ID	Bioabsorbable screw	Metal screw	Randomised site (s)	Other site	Type of graft	Other info
Arama 2015	PLLA with hydroxyapatite (HA-PLLA)	Titanium	Femur & tibia	N/A	Hamstrings	
Benedetto 2000	Copolymer of polyglycolic acid (PGA) and the elastomer trimethylene carbonate (PGA-TMC)	Titanium	Femur	Used bioabsorbable screw in both sites in 30 cases. Bio screw in the femur and metal screw in tibia in 24 cases. Bio screw in the femur with staples in the tibia in 13 cases. Metal screw in both sites in 41 cases. Metal screw in the femur with staples in the tibia in 16 cases	Patellar tendon	Tibial fixation was achieved with either the allocated screw or a standard fixation device
Drogset 2005	Poly-L-lactic acid (PLLA)	Not stated	Femur	The bone block in the tibial tunnel was fixed with an interference screw. Type of screw not stated	Patellar tendon	
Fink 2000	Copolymer of polyglycolic acid (PGA) and the elastomer trimethylene carbonate (PGA-TMC)	Titanium	Femur	Titanium screw.	Patellar tendon	
Hegde 2014	Not stated	Not stated	Tibia	Endobutton used for femur.	Hamstrings	"In all patients, femoral fixations were achieved by using endobuttons and tibial fixations were achieved by using

Table 1. Details of ACL reconstruction and interventions used in the included studies (*Continued*)

						either metallic or bioabsorbable interference screws, based on their randomisation."
Hofmann 2001	Poly-L-lactic acid (PLLA)	Titanium	Femur & tibia	N/A	Patellar tendon	Screw was made of Poly-L-lactide (98% L-lactide, 2% D-lactide)
Järvelä 2008	PLLA/TMC/PDLA	Titanium	Femur & tibia	N/A	Hamstrings	Poly-L-lactide, D-lactide, and trimethylene carbonate, bioabsorbable screw
Kaeding 2005	Poly-L-lactic acid (PLLA)	Titanium	Femur & tibia	N/A	Patellar tendon	
Kotani 2001	Poly-L-lactic acid (PLLA)	Titanium	Not stated	Not stated	Patellar tendon	
Laxdal 2006	Poly-L-lactic acid (PLLA)	Titanium	Femur & tibia	N/A	Hamstrings	
McGuire 1995	Poly-L-lactic acid (PLLA)	Titanium	Femur & tibia	States: "In 158 cases, a PLLA (n = 83) or metal screw (n = 75) was used to secure the graft on both ends. Staples (B = 17, M = 23) and screws with washers (B = 3, M = 2) were used to secure grafts at the tibial end in 45 reconstructions when Achilles tendons were used or when patella alta conditions were present. Those patients who had	Patellar tendon etc[1]	Separate data provided for patellar tendon group (Barber 1995 and Barber 2000)

Table 1. Details of ACL reconstruction and interventions used in the included studies (*Continued*)

				staples or screws with washers used for tibial fixation had a single interference screw inserted at the femoral end of their grafts. Augmentation by iliotibial band tenodesis was performed on 14 (B = 5, M = 9) patients." (McGuire 1999)		
Myers 2008	PLLA with hydroxyapatite (HA-PLLA)	Titanium	Femur & tibia	N/A	Hamstrings	

1. The data used in this review are from two trial reports presenting the results for the subgroup of participants who had patella tendon autografts. A report of the full trial listed 117 patella tendon autografts, 59 patella tendon allografts, 25 Achilles tendon allografts, and 3 combination autologous/allogenic grafts.

CONTRIBUTIONS OF AUTHORS

Pedro Debieux, Mario Lenza, Carlos Franciozi and Marcel Jun Tamaoki conceived and drafted the protocol and review. Mario Lenza, João Carlos Belloti, Flavio Faloppa, and Robert A Magnussen reviewed the review and provided input on methodological issues. Pedro Debieux, Carlos Franciozi and Marcel Jun Tamaoki helped find articles related to the review.

Pedro Debieux is the guarantor of this review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Universidade Federal de São Paulo, Brazil.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Types of outcome measures

We clarified that our top primary outcome was 'subjectively-rated knee function', with an emphasis on the use of validated patient-rated scores. While these scores may include a quality of life aspect, we split off knee function from general quality of life outcome measures, such as the SF-36. We made the latter a new secondary outcome.

We included arthrofibrosis, cyclops lesion and adhesions that required further surgery as named adverse events.

In the protocol, we planned to assess outcomes in the short term (within six months of ACL reconstruction), intermediate term (between six months and two years of ACL reconstruction), and long term (more than two years after ACL reconstruction). However, based on the distribution of data, we decided in the review to present the follow-up at one year, two years and over two years (long-term results).

Unit of analysis issues

There were no unit of analysis issues relating to the inclusion of people with bilateral ACL reconstruction. However, we made explicit our awareness of other unit of analysis issues, such as those relating to the use of more than one screw per knee and measurement of outcomes at different times.

Data analysis

Instead of expressing estimate effects as the number needed to treat for an additional beneficial outcome (NNTB) or the number needed to treat for an additional harmful outcome (NNTH) as in our protocol, we opted for the approach taken in the 'Summary of findings' table.

Because of inconsistencies present in included studies, we did not carry out our plan to investigate the potential impact of missing data on the findings of the review or conduct worst- and best-case scenario analyses.

INDEX TERMS

Medical Subject Headings (MeSH)

*Absorbable Implants [adverse effects]; *Anterior Cruciate Ligament Injuries; *Bone Screws [adverse effects]; Anterior Cruciate Ligament Reconstruction [instrumentation; *methods]; Joint Instability [etiology]; Knee Joint; Metals [adverse effects]; Patellar Ligament [transplantation]; Randomized Controlled Trials as Topic; Range of Motion, Articular; Tendons [*transplantation]; Treatment Outcome

MeSH check words

Humans